PDE5i & LA MALATTIA DI LA PEYRONIE

Francesco Varvello *MD, FEBU, FECSM*
Enrico Conti *MD, FECSM*

ASL CN2

S.C. Urologia
Ospedale “San Lazzaro”
Alba

Sicurezza

Strategia

Terapia

Riabilitazione

Sicurezza

I prodotti indicati per il trattamento della disfunzione erettile, incluso il sildenafil, devono essere impiegati con cautela nei pazienti con deformazioni anatomiche del pene (es. angolazione, fibrosi cavernosa o malattia di Peyronie).

Treatment of erectile dysfunction in patients with Peyronie's disease using sildenafil citrate

LA Levine[1]* and KC Latchamsetty[1]

2002

Sildenafil ha consentito rapporti penetrativi al 70% dei pazienti trattati

Nessun paziente ha riportato un aumento del dolore penieno.

Lo studio non evidenzia che le erezioni e i coiti consentiti dall'utilizzo di sildenafil abbiano prodotto un peggioramento delle deformità del pene o la progressione della malattia

Non appare esistere nessuna controindicazione all'utilizzo di sildenafil dal momento che rappresenta la terapia per la disfunzione erettile meno invasiva e più conveniente per i paziente affetti da malattia di Peyronie.

SCHEDE TECNICHE

SILDENAFIL, VARDENAFIL, AVANAFIL

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TADALAFIL

Deve essere impiegato con cautela nei pazienti con deformazioni anatomiche del pene (es. angolazione, fibrosi cavernosa o malattia di Peyronie).

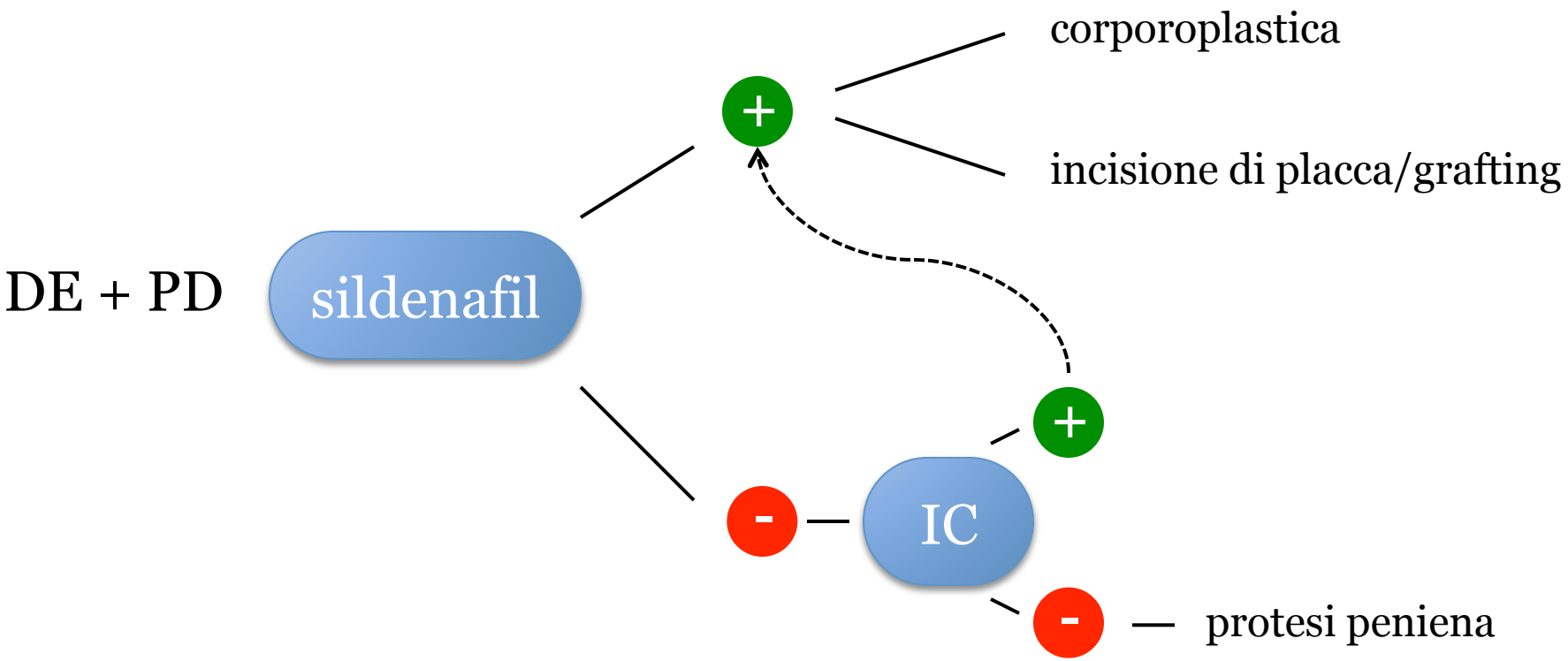
Strategia

2005

ORIGINAL RESEARCH—SURGERY

A Surgical Algorithm for Men with Combined Peyronie's Disease and Erectile Dysfunction: Functional and Satisfaction Outcomes

John Mulhall,* Matthew Anderson,† and Marilyn Parker†



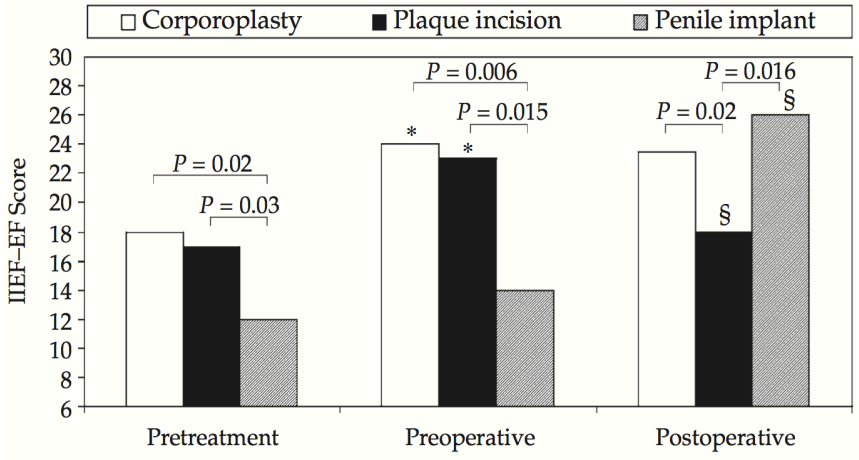
2005

ORIGINAL RESEARCH—SURGERY

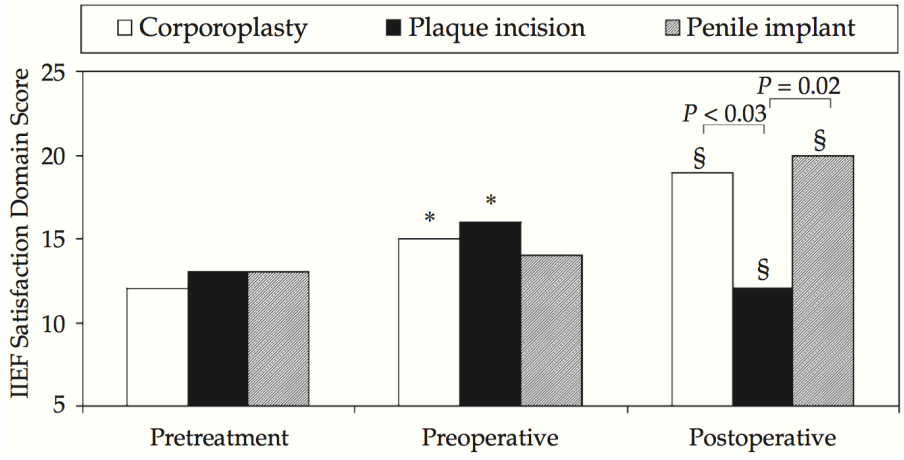
A Surgical Algorithm for Men with Combined Peyronie's Disease and Erectile Dysfunction: Functional and Satisfaction Outcomes

John Mulhall,* Matthew Anderson,† and Marilyn Parker†

IIEF



soddisfazione



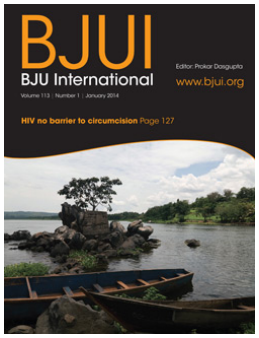
2012

Predicting Erectile Dysfunction Following Surgical Correction of Peyronie's Disease without Inflatable Penile Prosthesis Placement: Vascular Assessment and Preoperative Risk Factors

Frederick L. Taylor, MD,* Michael R. Abern, MD,† and Laurence A. Levine, MD†

Factor	Average values (ED)	Average values (no ED)	*P* value
Plication vs. Grafting	—	—	0.12
Resistive index	0.919	0.92	0.86
Peak systolic velocity	37.9	35.8	0.66
End diastolic velocity	2.25	2.52	0.34
History of tobacco use	30%	34%	0.99
Chronic hypertension	23%	14%	0.51
Diabetes mellitus	7%	3%	0.69
Hyperlipidemia	25%	20%	0.87
Graft area (cm^2)	22	21	0.56
Preoperative use of phosphodiesterase type 5 inhibitors	44%	44%	0.33

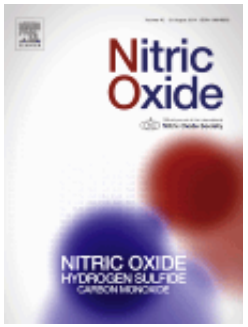
Terapia



1998

Histological and ultrastructural alterations in an animal model of Peyronie's disease

El-Sakka AI, Hassan MU, Nunes L, Bhatnagar RS, Yen TS, Lue TF



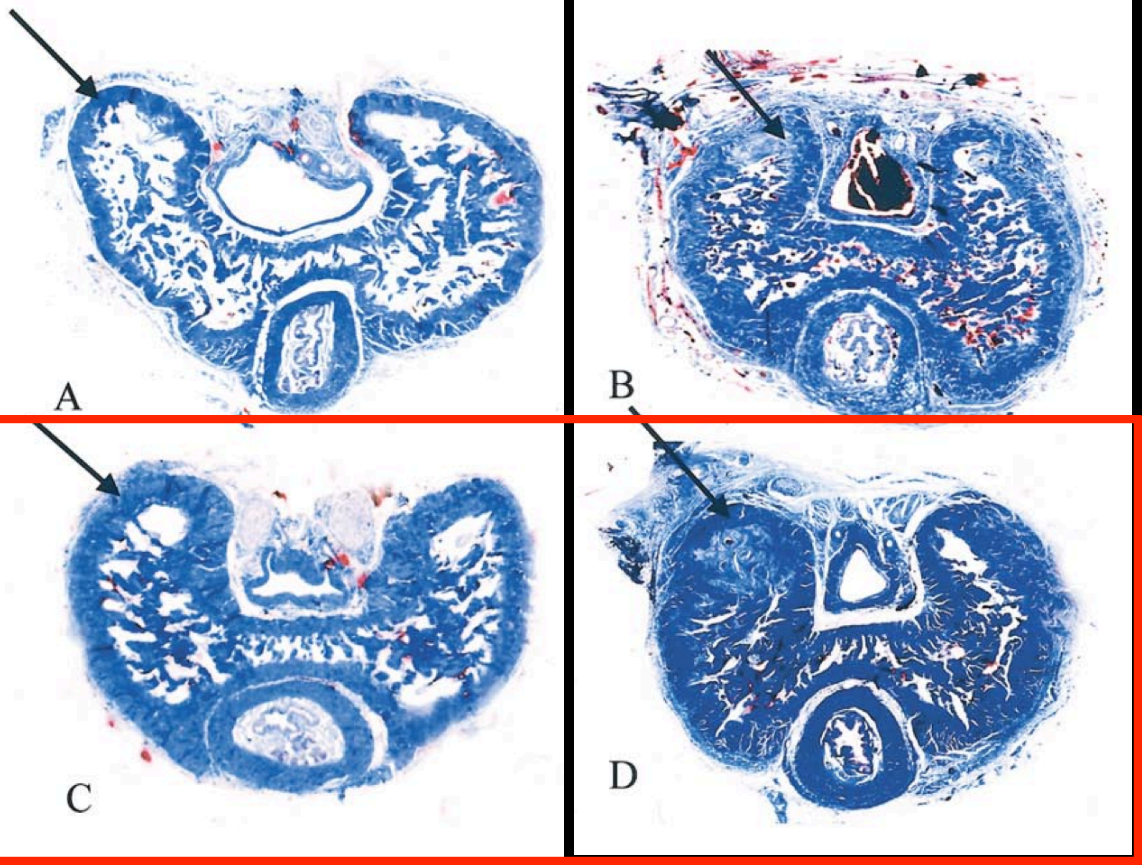
Antifibrotic Role of Inducible Nitric Oxide Synthase

M. G. Ferrini, D. Vernet, T. R. Magee, A. Shahed, A. Qian, J. Rajfer, and N. F. Gonzalez-Cadavid[1]

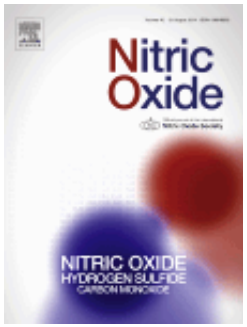
Department of Urology, UCLA School of Medicine, Los Angeles, California; and Division of Urology, Research and Education Institute, Harbor-UCLA Medical Center, Torrance, California

2002

TGFb



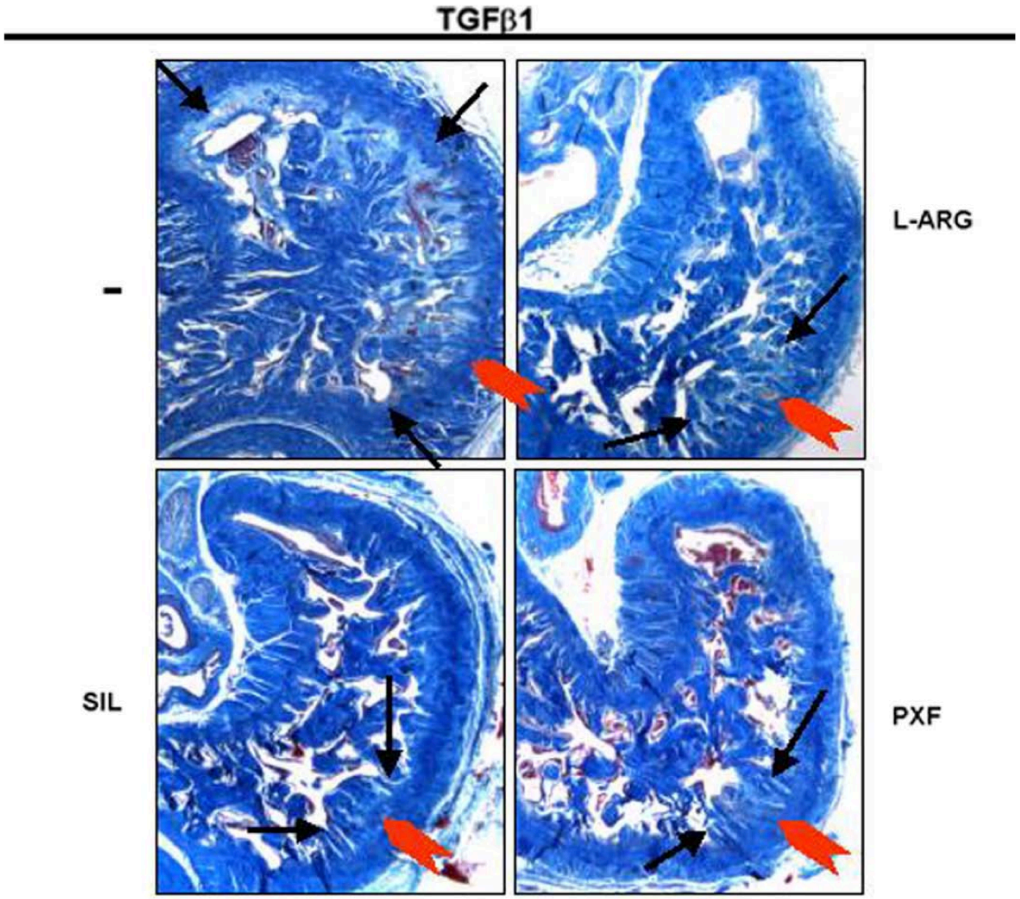
inibitore
iNOS

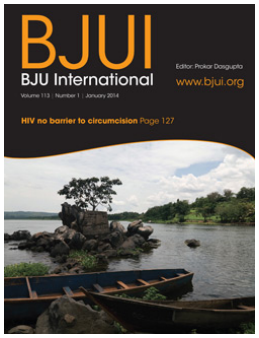


2003

L-Arginine and phosphodiesterase (PDE) inhibitors counteract fibrosis in the Peyronie's fibrotic plaque and related fibroblast cultures

Eliane G.A. Valente,[a,1] Dolores Vernet,[a,1] Monica G. Ferrini,[a,1] Ansha Qian,[a] Jacob Rajfer,[a,b] and Nestor F. Gonzalez-Cadavid[a,b,*]

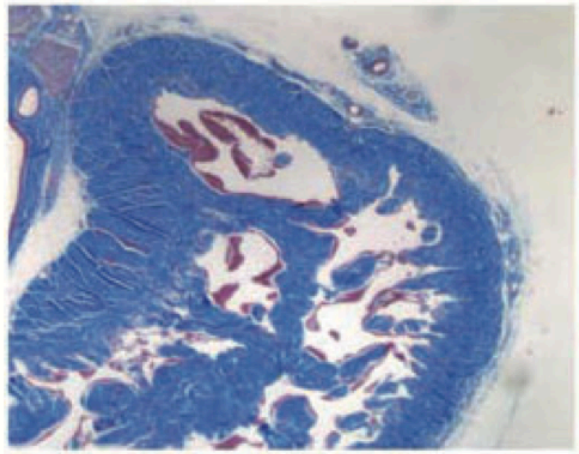




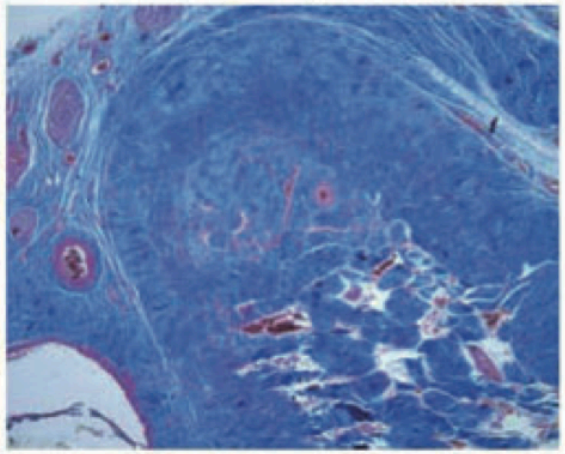
2006

Effects of long-term vardenafil treatment on the development of fibrotic plaques in a rat model of Peyronie's disease

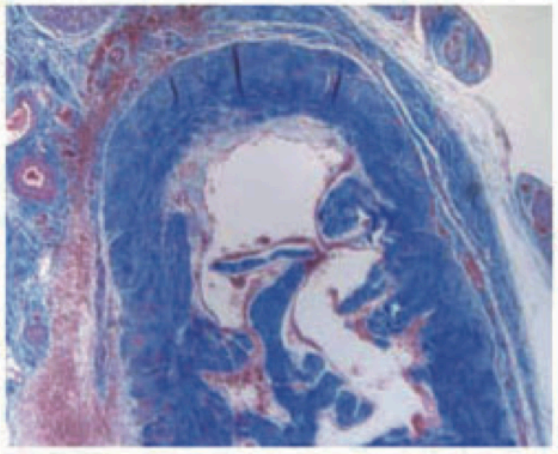
MONICA G. FERRINI*†, ISTVAN KOVANECZ*, GABY NOLAZCO*, JACOB RAJFER*† and NESTOR. F. GONZALEZ-CADAVID*†
Division of Urology, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA, and †Department of Urology, UCLA David Geffen School of Medicine, Los Angeles, CA, USA



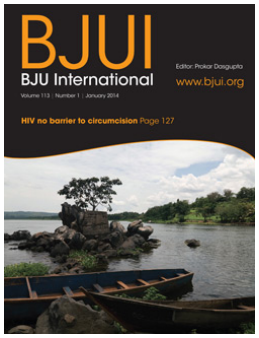
Control-saline (Group 1)



TGF-β1 (Group 2)



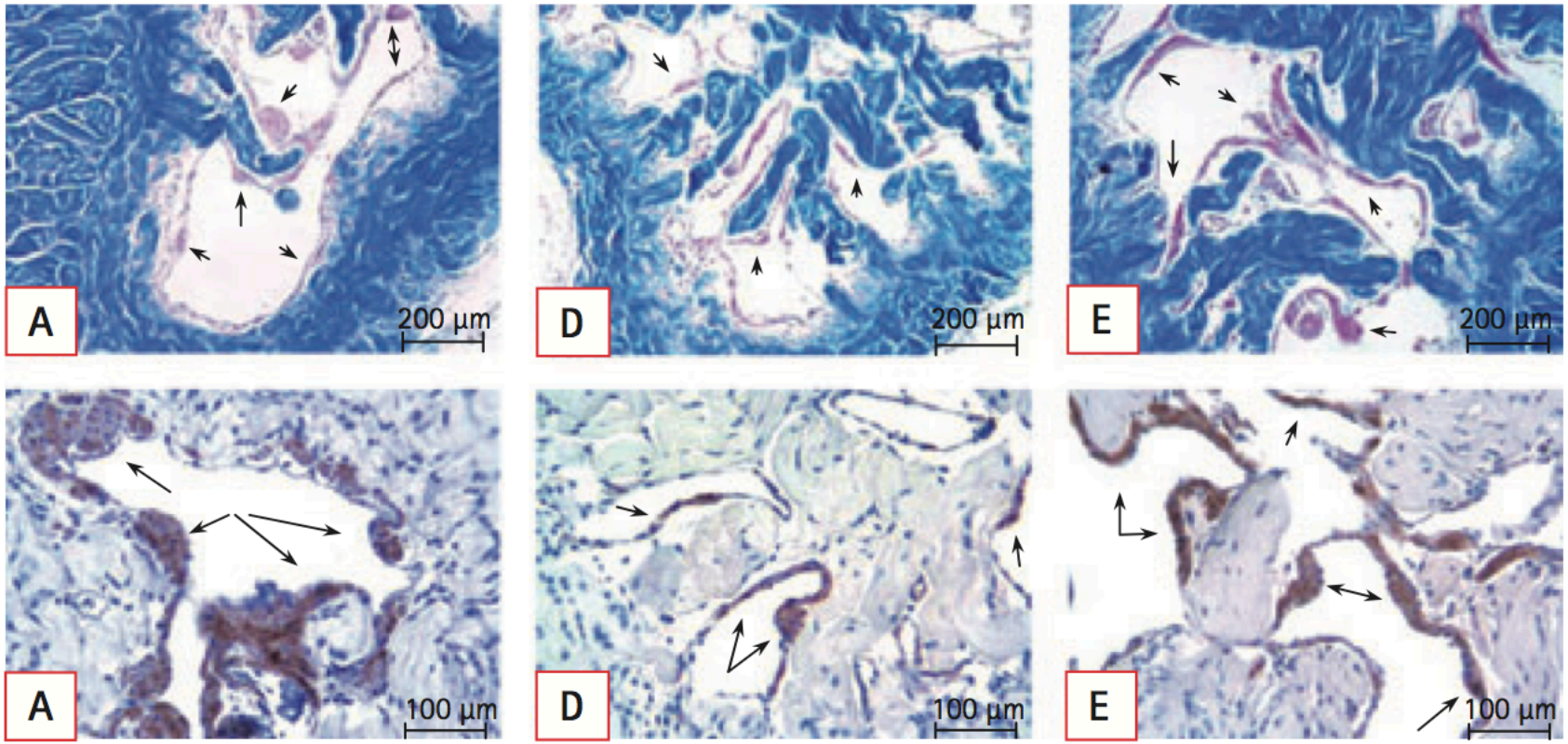
TGF-β1 + vardenafil (Group 4)



2008

Chronic daily tadalafil prevents the corporal fibrosis and veno-occlusive dysfunction that occurs after cavernosal nerve resection

Istvan Kovanecz*, Amarnath Rambhatla*, Monica G. Ferrini*‡, Dolores Vernet*, Sandra Sanchez*, Jacob Rajfer*†‡ and Nestor Gonzalez-Cadavid*†‡



The Role of PDE5 Inhibitors in Penile Septal Scar Remodeling: Assessment of Clinical and Radiological Outcomes

Eric Chung, MD, Ling DeYoung, MD, and Gerald B. Brock, MD

Division of Urology, St Joseph Health Care, London, Ontario, Canada

2011

6 mesi

tadalafil

2,5 mg
daily

6 mesi

placebo

daily

69%

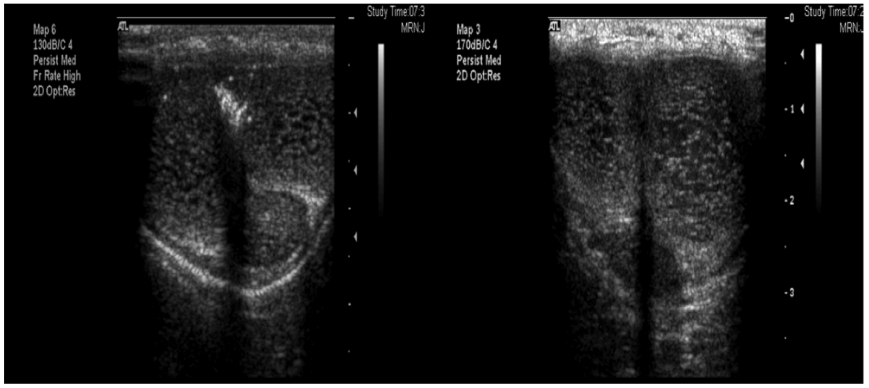
10%

risoluzione della placca
p<0,05

65 pz

Retrospettivo

Solo placche settali isolate, non palpabili, senza deformità dell'asta



2014

ORIGINAL ARTICLE

Effects of sildenafil treatment on patients with Peyronie's disease and erectile dysfunction

U. Ozturk · S. Yesil · H. N. G. Goktug · A. Gucuk · C. Tuygun · N. C. Sener · I. Nalbant · M. A. Imamoglu

39 pz

12 settimane di trattamento

18 pz

Vit E

400 UI daily

33% risoluzione della placca

43% risoluzione del dolore

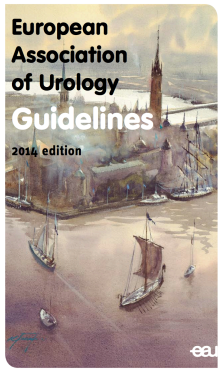
21 pz

sildenafil

50 mg daily

33% risoluzione della placca

66% risoluzione del dolore



2014

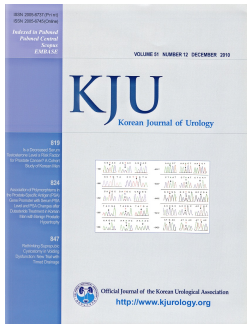
Guidelines on
Penile Curvature

first introduced
2012

E. Wespes (chair), K. Hatzimouratidis (vice-chair), I. Eardley,
F. Giuliano, D. Hatzichristou, I. Moncada, A. Salonia, Y. Vardi

4.3.1.7 Phosphodiesterase type 5 inhibitors

The rationale for the use of phosphodiesterase type 5 inhibitors (PDE5I) in Peyronie's disease comes from animal studies showing that they can reduce the collagen/smooth muscle and collagen III/I ratios and increase the apoptotic index in the Peyronie's disease-like plaque (64). In a retrospective controlled study, daily tadalafil (2.5 mg for 6 months) resulted in statistically significant ($p < 0.05$) resolution of septal scar in 69% of patients compared to 10% in the control group (no treatment). However, this study included patients with isolated septal scars without evidence of penile deformity (65). Therefore, no recommendation can be given for PDE5I in patients with Peyronie's disease.



Urologists' Perceptions and Practice Patterns in Peyronie's Disease: A Korean Nationwide Survey Including Patient Satisfaction

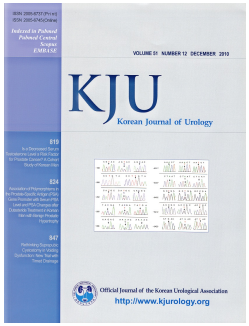
Young Hwii Ko, Ki Hak Moon, Sung Won Lee[1], Sae Woong Kim[2], Dae Yul Yang[3], Du Geon Moon[4], Woo Sik Chung[5], Kyung Jin Oh[6], Jae Seog Hyun[7], Ji Kan Ryu[8], Hyun Jun Park[9], Kwangsung Park[6]

2014

Contattati 2400 urologi koreani

385 questionari compilati

Terapia orale preferita in primo approccio:



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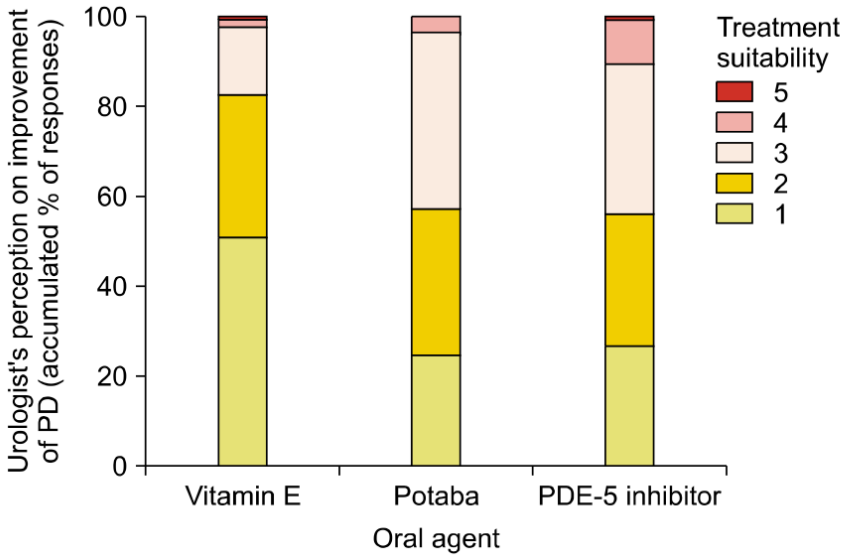
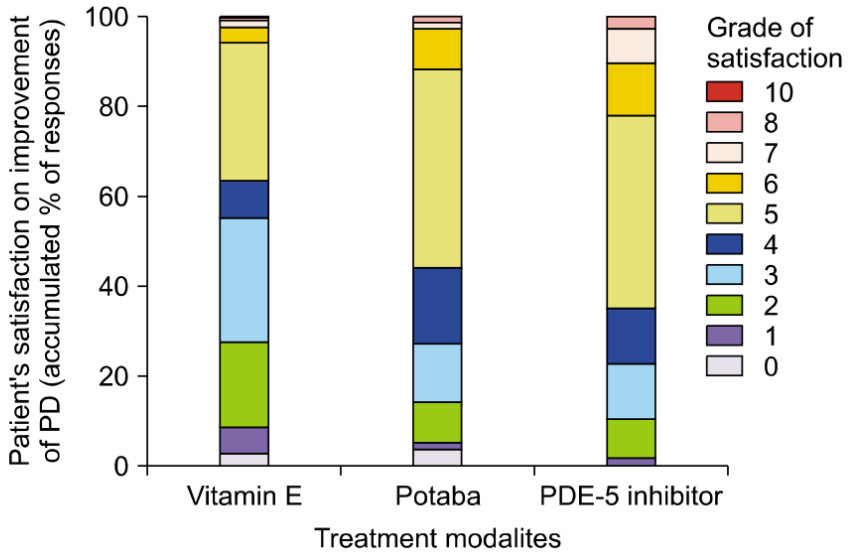
2014





TheScientificWorldJOURNAL
www.thescientificworld.com

2009

Peyronie's Disease: Evolving Surgical Management and the Role of Phosphodiesterase 5 Inhibitors

Tariq F. Al-Shaiji* and Gerald B. Brock
Division of Urology, Department of Surgery, University of Western Ontario, London, ON

Non ci sono studi pubblicati che esaminano il ruolo dei PDE5i nella dissoluzione delle placche di IPP in un setting clinico.

Nel nostro centro abbiamo notato, in maniera aneddotica, alcuni miglioramenti soggettivi e oggettivi in uomini con malattia di Peyronie trattati in cronico con tadalafil a basse dosi.

2013

CASE REPORT

Peyronie's disease: A "triple oxygenant therapy"

Francesco Ciociola [1], Giovanni Maria Colpi [2]

[1] Specialista in Endocrinologia e Malattie del Ricambio - Consulente Andrologo - U.O.C. Urologia 2 - Andrologia e Riproduzione Assistita, Azienda Ospedaliera San Paolo - Polo Universitario, Milano, Italy;
[2] Specialista in Andrologia, Urologia ed Endocrinologia - Direttore U.O.C. Urologia 2 - Andrologia e Riproduzione Assistita, Azienda Ospedaliera San Paolo - Polo Universitario, Milano, Italy.

pz 20 anni
placca fibrotica al terzo medio dell'asta da 3 settimane
modesto dolore
regolare funzione erettile

verapamil topico + ionoforesi 2/settimana
>>> incurvamento dell'asta, deformazione a clessidra, accorciamento

verapamil intralesionale 5 mg per 8 settimane + penile extender 6 ore/giorno
>>> persistenza di placca palpabile a livello settale

2013

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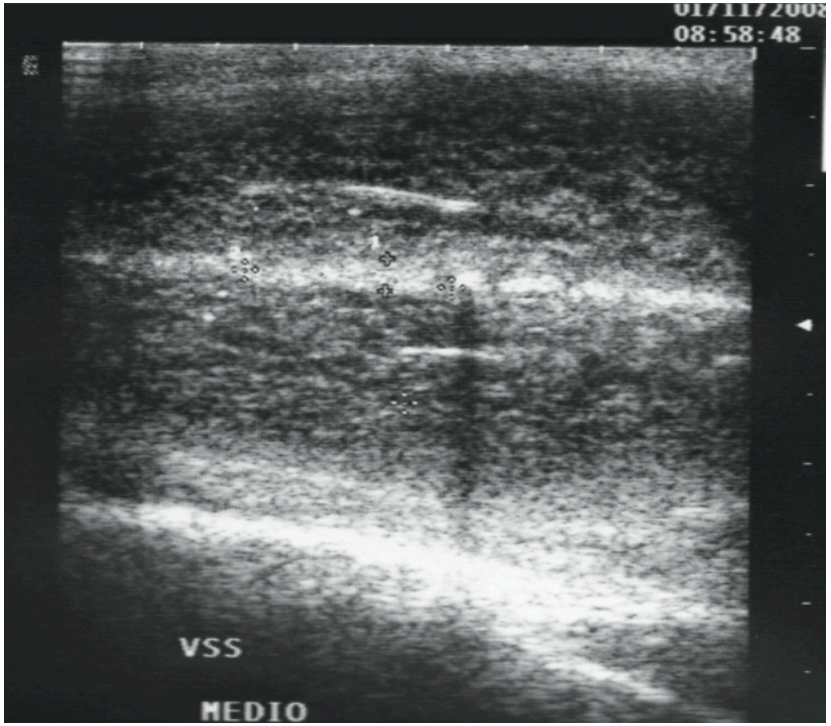
placca settale
13.6 x 2.3 mm

dimensioni pene
lunghezza 11.5 cm
larghezza 11.5 cm



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pentossifillina 400 mg x 3/giorno
tadalafil 5 mg 3/settimana
levo-arginina 2500 mg
propionil-carnitina 250 mg } /giorno
vitamina B3 20 mg

penile extender 6 ore/giorno

per 2 anni

2013

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[1] Specialista in Endocrinologia e Malattie del Ricambio - Consulente Andrologo - U.O.C. Urologia 2 - Andrologia e Riproduzione Assistita, Azienda Ospedaliera San Paolo - Polo Universitario, Milano, Italy;
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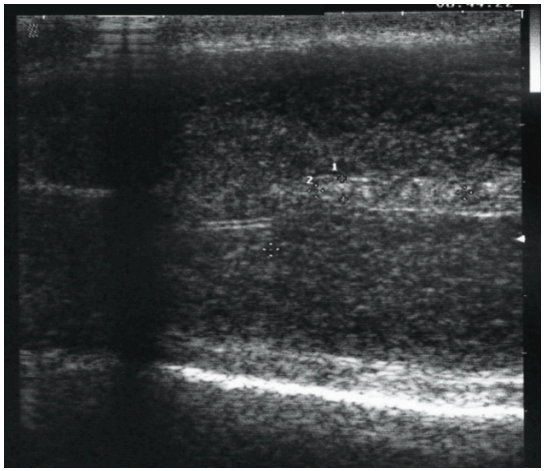
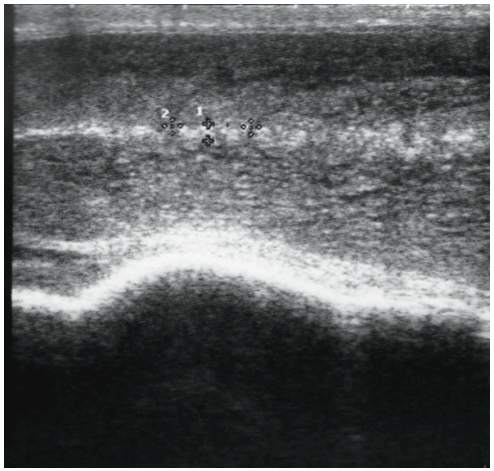
dopo 1 anno



placca settale **ipoecogena 12.4 x 1.9 mm**
più soffice alla palpazione
lunghezza pene **14 cm**, larghezza **12.5 cm**

dopo 2 anni



placca settale **7 x 1.6 mm**
lunghezza e larghezza pene invariati

2013

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Non è possibile escludere una remissione spontanea della fibrosi settale

NO-iNOS coinvolti nella modulazione della fibrosi nella malattia di Peyronie

Up-regulation di NO-cGMP può prevenire e ridurre la fibrosi della tunica albuginea

L'uso del penile extender permette di aumentare/recuperare le dimensioni e rinforza l'effetto farmacologico

Riabilitazione

PRINCIPALI LAMENTELE DOPO CHIRURGIA PER MALATTIA DI PEYRONIE

Accorciamento

Persistenza della curvatura

Riduzione della sensibilità

Disfunzione erettile

	Tunical shortening procedures		Tunical lengthening procedures
	Nesbit	**Plication**	**Grafts**
Penile shortening	4.7-30.8%	41-90%	0-40%
Penile straightening	79-100%	58-100%	74-100%
Persistent or recurrent curvature	4-26.9%	7.7-10.6%	0-16.7%
Post-operative erectile dysfunction	0-13%	0-22.9%	0-15%
Penile hypoesthesia	2-21%	0-21.4%	0-16.7%
Technical modifications	1	At least 3	Many types of grafts and techniques used

Nesbit/plicature DE 4-13%

Grafting DE 5-53%

Taylor FL, et al. JSM 2012; 9:296-301.

FATTORI LEGATI ALL'ETA' E ALLA MALATTIA

Fibrosi indotta dall'ipossia, ipotestosteronemia.

Riduzione della percentuale di tessuto muscolare liscio

Scompaginamento della struttura del corpo cavernoso nella malattia di Peyronie

Disfunzione erettile pre-esistente
Età >60 anni
Curvatura ventrale

} fattori predisponenti

Moreland et al. Int J Impot Res 1998; 10: 113
Wespes et al. J Urol 1997; 157:1678
El Sakka et al. J Androl 2010; 31: 324
Mulhall et al. JSM 2005; 2: 132

FATTORI LEGATI ALLA CHIRURGIA

Il trauma chirurgico “di per se” non rappresenta un fattore di rischio

Le alterazioni post-chirurgiche della sensibilità possono concorrere (2-36%) alla determinazione della DE

Chirurgia complessa

Dimensioni del graft

El Sakka et al. Br J Urol 1998; 159: 1700
Ralph et al. JSM 2010; 7: 2359
Chung et al. JSM 2011; 8: 594
Mulhall et al. JSM 2005; 2: 132

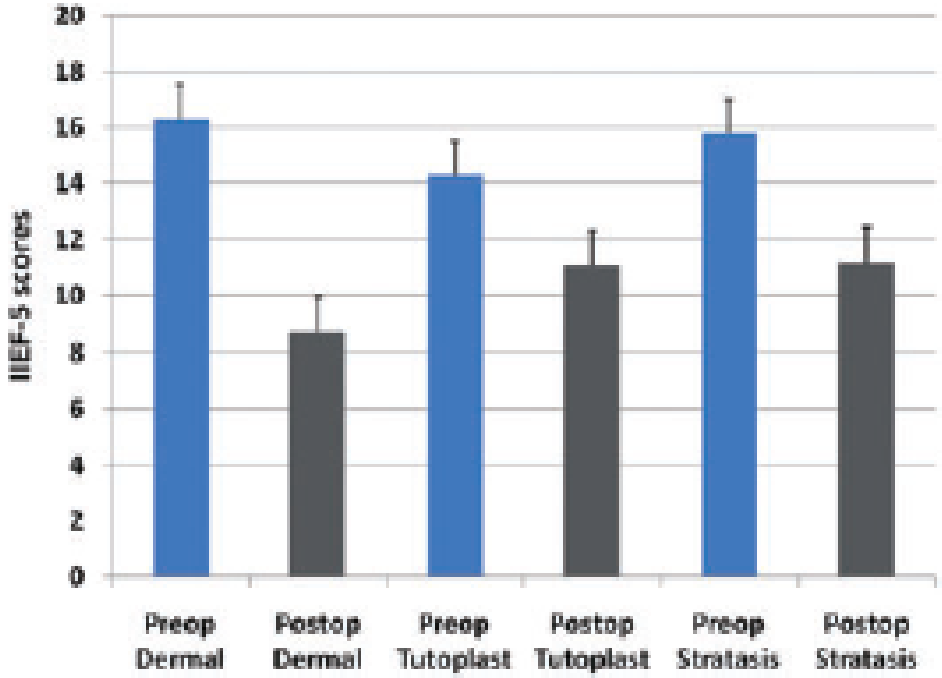
2011

Five-Year Follow-Up of Peyronie's Graft Surgery: Outcomes and Patient Satisfaction

Eric Chung, FRACS,* Eric Clendinning,† Lauren Lessard,† and Gerald Brock, MD*

*St Joseph Health Care—Urology, London, Ontario, Canada; †University of Western Ontario, London, Ontario, Canada

DOI: 10.1111/j.1743-6109.2010.02102.x



Esiste un razionale per l'utilizzo dei PDE5i nella riabilitazione dei pazienti sottoposti a chirurgia peniena per malattia di Peyronie?

2011

Erectile Dysfunction Following Surgical Correction of Peyronie's Disease and a Pilot Study of the Use of Sildenafil Citrate Rehabilitation for Postoperative Erectile Dysfunction

Laurence A. Levine, MD, Jason M. Greenfield, MD, and Carlos R. Estrada, MD

Section of Urology, Rush University Medical Center, Chicago, IL, USA

1 mese

26 pz — sildenafil — **26%**

25 mg
nightly

DE postoperatoria

11 pz — nessun trattamento — **36%**

2010

Special Article
Arch. Esp. Urol. 2010; 63 (9): 755-770

CURRENT SURGICAL MANAGEMENT OF SEVERE PEYRONIE'S DISEASE

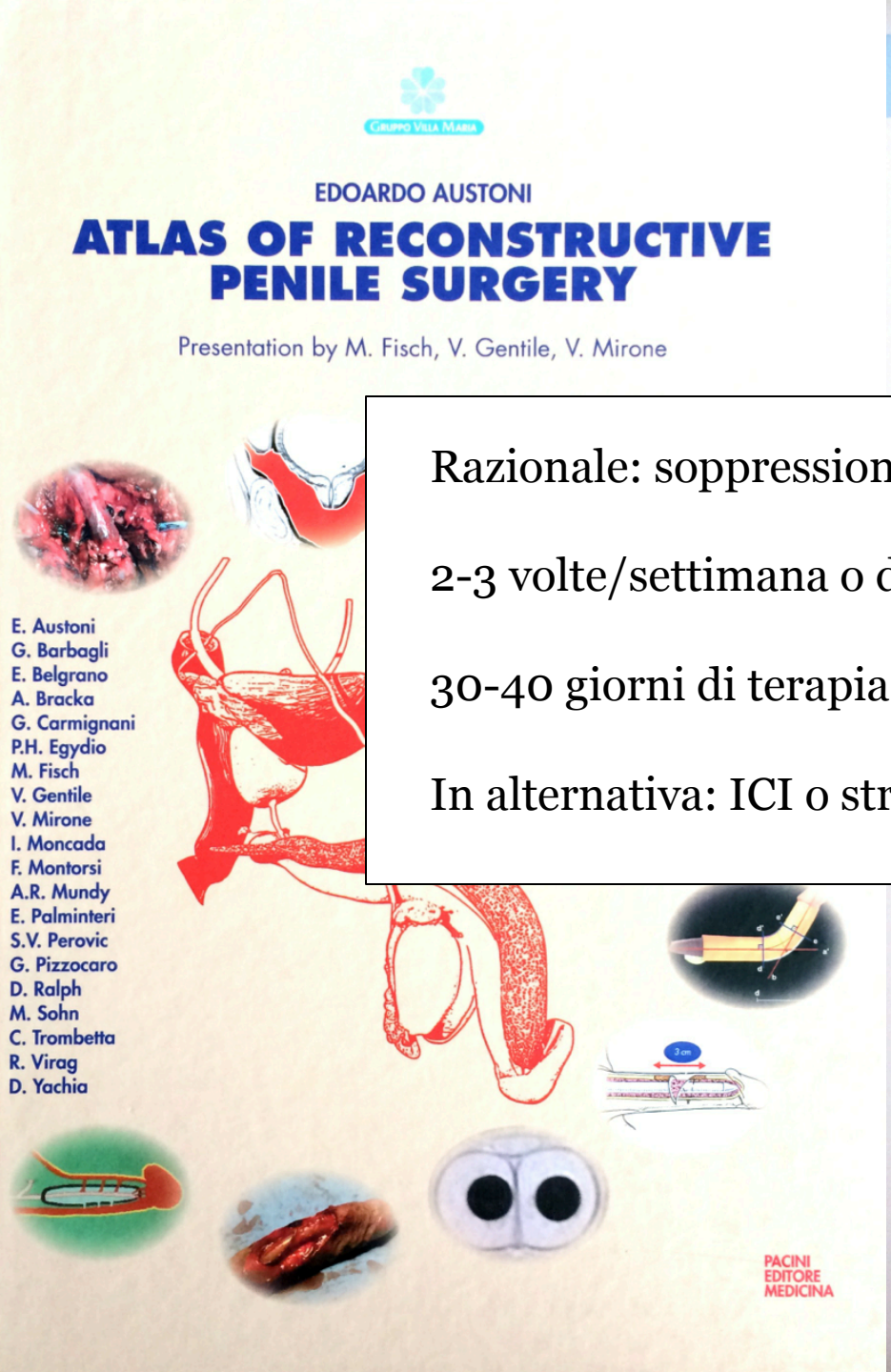
Sava V. Perovic† and Rados P. Djinovic[1].

Serbian Academy of Sciences and Arts. Belgrade. Serbia
[1]School of Medicine. University of Belgrade. Serbia.

Postoperative physiotherapy

Daily PDE5 inhibitors are prescribed for 3-4 weeks starting 2-3 days after surgery in order to induce erections and increase penile blood flow. Patients are advised to use of penile stretching device approximately 2-3 weeks postoperatively and vacuum device 1-2 weeks later to prevent graft shrinkage and consequent penile shortening and re-curvature. Physiotherapy was applied for 4-6 months after surgery.

We also advised using of vacuum device in patients with penile prosthesis implantation.



SEXUAL REHABILITATION AFTER PENILE RECONSTRUCTIVE SURGERY

Vincenzo Gentile, Gabriele Antonini
Sapienza University of Rome, Italy

ch and maintain a sufficiently valid erec-
haemodynamic event induced by relaxa-
d by neurotransmitters (NO, PGE1, VIP,
ystem (S2-S4) which, in turn, is stimulated
particular, by the paraventricular nucleus

cular vascularisation of the penis and is
flaccid conditions, the blood flows to the
ay, through the veins. In the case of erec-
ase in arterial flow and blockage of the

gical aesthetic treatment, functional and/

l approach and use of materials which
s a possible complication which severely
surgery.
ese patients, is two-fold:

e penis (anti-fibrotic action).
h the pre-operative situation and age of
-pathological mechanisms of secondary
avernosal bodies is mandatory in order

to avoid fibrotic processes. The steps to rehabilitation should be commenced approximately 25-30 days after the surgical treatment.

Treatment of ED has been revolutionized with the introduction of PDE5 inhibitors (PDE5i) and has paved the way for the rehabilitation concept in patients submitted to penile and prostatic surgery. Phosphodiesterase-5 (PDE5) is the enzyme responsible for catabolism of cGMP (cyclic monophosphate guanosine) produced in the smooth muscle fibre cells following their activation triggered by nitrogen monoxide. Administration of PDE5 inhibitors (PDE5i) is important in patients with ED in order to improve not only erectile function, but also systemic endothelial function. Furthermore, as demonstrated in numerous studies, it is possible to use chronic treatment with PDE5i, which have been shown to be more effective than *on-demand* treatments in improving this parameter (De Sousa, 2002; Rosano, 2005; Aversa, 2007; Sommer, 2005; Caretta, 2005). Pharmacological treatment in sexual rehabilitation following penile surgery has, furthermore, been found to be better accepted by the patients themselves inasmuch as it is non-invasive. Besides sildenafil, other agents with the same mechanism of action (tadalafil, vardenafil) are equally as efficacious. Tadalafil, in particular, presents certain pharmacological characteristics (long half-life) making it potentially the drug of choice in the rehabilitation phase. Suppression of the TGF β1-mediated collagen synthesis, especially at smooth muscle cell level, is the patho-physiological mechanism upon which the rehabilitative function of the inhibitors is based. Good condition of the nerves is, however, necessary, in order

Razionale: soppressione dell'attività del TGFb

2-3 volte/settimana o daily

30-40 giorni di terapia

In alternativa: ICI o stretching con vacuum

2010

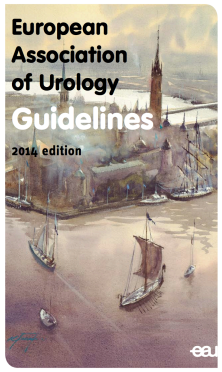
The Management of Peyronie's Disease: Evidence-based 2010 Guidelines

David Ralph, MD,* Nestor Gonzalez-Cadavid, PhD,† Vincenzo Mirone, MD,‡ Sava Perovic, MD,§ Michael Sohn, MD,¶ Mustafa Usta, MD,** and Laurence Levine, MD††

*Institute of Urology, London UK; †Department Urology, UCLA, CA, USA; ‡University of Naples "Federico II", Naples, Italy; §University of Belgrade, Belgrade, Serbia; ¶University Aachen, Germany; **Akdeniz University School of Medicine, Antalya, Turkey; ††Rush Medical College, Chicago, IL, USA

Postoperative Care and Rehabilitation

Following surgery, postoperative rehabilitation is recommended to enhance recovery of erectile function. Massage and stretch therapy, is performed by grasping the glans penis and pulling it gently and repeatedly away from the body while also gently massaging the graft area. This is initiated 2 weeks after surgery and performed twice a day for 4 weeks. It is advised that the patient's partner get involved in the rehabilitation process to lessen the anxiety associated with the resumption of sexual activity for both partners. Bedtime phosphodiesterase inhibitors have been recommended to begin 7–10 days after surgery and to be maintained for 6 weeks, in order to enhance nocturnal erections, stretch the tissue, encourage nourishment of the graft [159], and possibly reduce the risk of postoperative ED. Finally, the use of external penile traction therapy has been noted to reduce postoperative penile shortening for patients who have undergone either placation or grafting procedures. Traction is initiated 2–3 weeks postoperatively when the circumcising incision has adequately healed and is performed on a daily basis for a minimum of 2–8 hours for 3 months [181].



Guidelines on
Penile Curvature

first introduced
2012

E. Wespes (chair), K. Hatzimouratidis (vice-chair), I. Eardley,
F. Giuliano, D. Hatzichristou, I. Moncada, A. Salonia, Y. Vardi

2014

4.4.2 *Penile lengthening procedures*

Tunical incision, preferably with grafting, offers an excellent surgical option for men with curvatures over 60° as well as patients with an hourglass deformity and good erectile function that are willing to risk a higher rate of postoperative erectile dysfunction (139). The presence of pre-operative erectile dysfunction, the use of larger grafts, age more than 60 years, and ventral curvature are considered poor prognostic factors for functional outcome after grafting surgery (106). Although the risk for penile shortening is significantly less compared to the Nesbit or plication procedures, it is still an issue and patients must be informed accordingly (104). The use of a penile extender device on an 8- to 12-hour daily regimen has been advocated as an effective and safe way to the loss of penile length in patients operated on for Peyronie's disease (140).

Maggio 2012

INTERVISTA AI SOCI SIA

5 domande

44 colleghi hanno restituito il questionario

Questionario

1) Eseguite presso il vostro centro interventi di corporoplastica?
Si
No

2) Eseguite presso il vostro centro interventi di uretroplastica?
Si
No

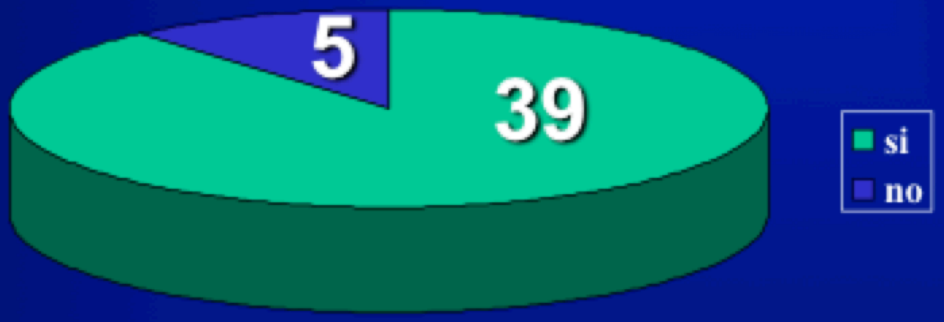
3) Se si, quale tipologia di interventi eseguite:
- correzione di recurvatum congeniti con patch
- correzione di recurvatum congeniti con Nesbit e varianti
- correzione di recurvatum da IPP (Nesbit e varianti)
- correzione di recurvatum da IPP (patch)
- uretroplastica (ogni tipologia)

4) Nel postoperatorio utilizzate farmaci per la riabilitazione della funzione erettile?
- PDE5i
- alprostadil
- alprostadil + PDE5i
- altro
- no

5) Se pratichi tale riabilitazione quale pensi sia il razionale alla base? (inserire breve commento)

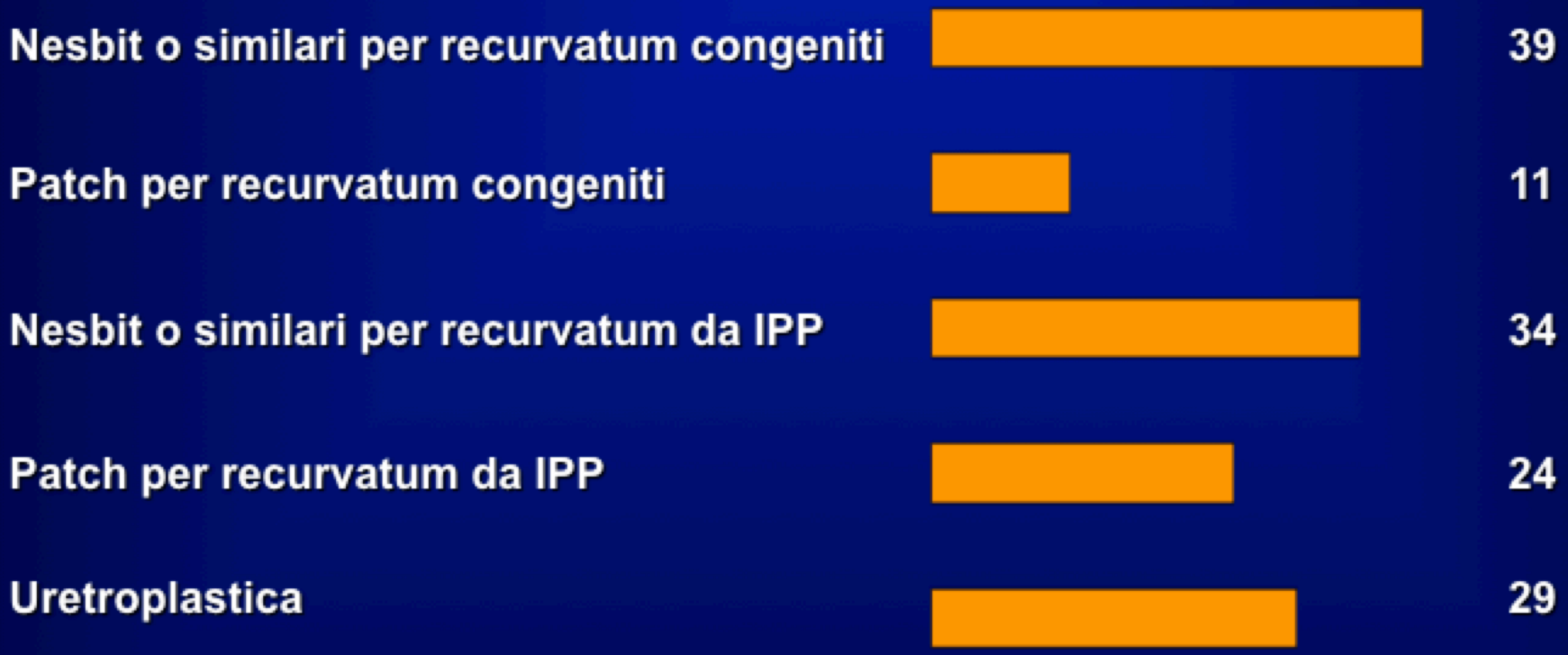

AUSTRIA
UNGHERIA
SVIZZERA
SLOVENIA
CROAZIA
BOSNIA-ERZEGOVINA
LIECHTENSTEIN
MONACO
SAN MARINO
CITTÀ DEL VATICANO
Corsica
SARDEGNA
SICILIA
TOSCANA
UMBRIA
MOLISE
BASILICATA
CALABRIA
Mar Ligure
Mar Adriatico
Mar Tirreno
Mar Ionio
MEDITERRANEO
Milano Più di 1 000 000 di abitanti
Verona Da 250 000 a 1 000 000 di abitanti

Eseguite presso il vostro centro interventi di corporoplastica?



Eseguite presso il vostro centro interventi di uretroplastica?

Se si, quale tipologia di interventi eseguite?



Nel postoperatorio utilizzate farmaci per la riabilitazione della funzione erettile?

Se pratichi tale riabilitazione quale pensi sia il razionale alla base?

Prevenzione fibrosi e retrazione	8
Stretching	7
Vasodilatazione	5
Ossigenazione	4
Favorire recupero funzione erettile	6
Stimolare le erezioni spontanee	3
Migliorare la funzione endoteliale	3
Shock funzionale immediato	1
Accelerare istotrasformazione del patch	1
Prevenzione della disf. veno-occlusiva	1

Sicurezza — OK

Strategia — Non dimostrata utilità

Terapia
- Studi preclinici dimostrano un razionale
- Studi clinici insufficienti
- LG: nessuna raccomandazione
- Pratica clinica… variopinta!

Riabilitazione
- Esiste il razionale
- Studi clinici insufficienti
- LG e esperti ne consigliano l'uso
- Pratica clinica concorde

PDE5i & DISTURBI DELL'ORGASMO E DELL'EIACULAZONE

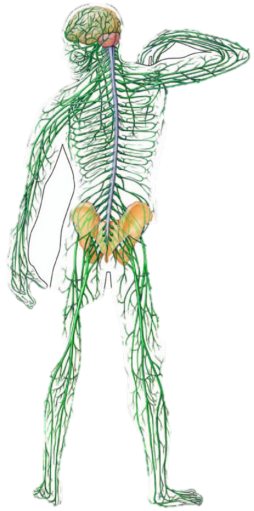
Francesco Varvello *MD, FEBU, FECSM*
Enrico Conti *MD, FECSM*

ASL CN2

S.C. Urologia
Ospedale "San Lazzaro"
Alba

& NO & PDE5i

• è stato dimostrato che le PDE5 sono espresse nel SNC
• in seguito a somministrazione di sildenafil sono descritti effetti nel SNC negli uomini
• i donatori di NO aumentano i livelli di cGMP nell'ipotalamo, e l'infusione di NO nell'ambiente extracellulare all'interno della MPOA dei ratti induce le erezioni e stimola il comportamento sessuale
• NO riduce le efferenze simpatiche alla periferia attraverso un meccanismo dipendente dal cGMP o attraverso interazioni con altri neurotrasmettitori
• la somministrazione intratecale di sildenafil nei ratti aumenta i livelli di NO e cGMP nella MPOA
• la riduzione del tono adrenergico mediata dall'attività del NO è in relazione con l'inibizione dell'eiaculazione
• la microiniezione di inibitori delle NOS riduce la latenza alla prima eiaculazione



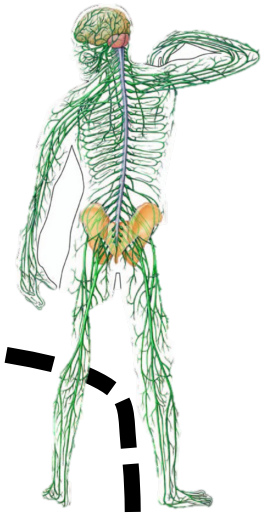
& NO & PDE5i

• NO e i donatori di NO inibiscono l'emissione del liquido seminale nei ratti
• gli inibitori di NO riducono la latenza eiaculatoria nei ratti
• l'innervazione mediata da NO e l'attività delle NOS sono state rilevate nei vasi deferenti, vescicole seminali, prostata e uretra
• l'attività delle PDE5 è stata rilevata nei vasi deferenti, vescicole seminali, prostata
• il sildenafil inibisce la trasmissione degli impulsi adrenergici nelle vescicole seminali umane
• il sildenafil ha un effetto inibitorio diretto sull'attività contrattile delle vescicole seminali

Neurotrasmissione NANC

PDE5i

NO



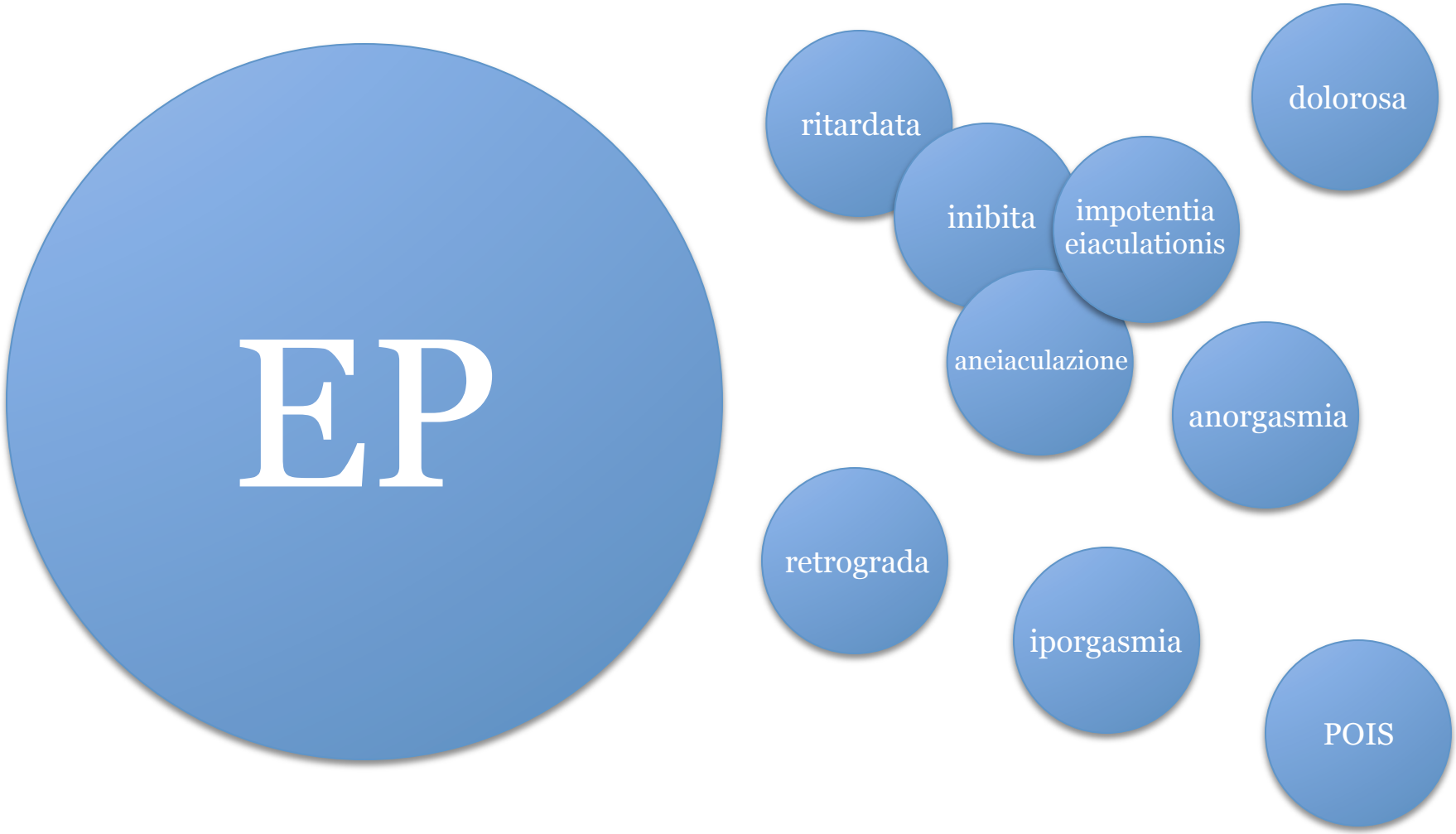
tono simpatico

analgesia periferica
erezione
controllo sull'eiaculazione
soddisfazione sessuale

ansia da prestazione
periodo refrattario

contrattilità deferenti e VS

vasocostrizione adrenergica



DISTURBI DELL'EIACULAZIONE E DELL'ORGASMO


lifelong
EP

&


PDE5i

2001

Assessment of as needed use of pharmacotherapy and the pause-squeeze technique in premature ejaculation

IA Abdel-Hamid[1]*, EA El Naggar[2] and A-H El Gilany[3]

[1]*Department of Andrology, Mansoura Faculty of Medicine, Mansoura, Egypt;* [2]*Department of Psychiatry, Mansoura Faculty of Medicine, Mansoura, Egypt; and* [3]*Department of Community Medicine, Mansoura Faculty of Medicine, Mansoura, Egypt*

	Baseline	*Clomipramine*	*Sertraline*	*Paroxetine*	*Sildenafil*	*Squeeze technique*	*Friedman* χ^2	*dF*	P
Anxiety score									
Median	12	11	11	9	8	12			
(Range)	(5–25)	(4–22)	(5–22)	(5–23)	(4–15)	(5–21)	55.15	5	0.0001
IVELT (min)									
Median	1	4	3	4	15	3			
(Range)	(0.5–1.5)	(1–8)	(1–10)	(2–10)	(5–30)	(1–7)	92.53	5	0.0001
Sexual satisfaction score									
Median		11	10	12	[illegible]	6			
(Range)		(0–25)	(0–31)	(0–29)	(17–34)	(0–22)	57.87	4	0.0001
IVELT during washout periods (min)									
Median		1	1	1	1.75	1			
(Range)		(0.5–1.5)	(0.5–2)	(0.5–2)	(0.5–8)	(0.5–1.5)	32.52	5	0.0001

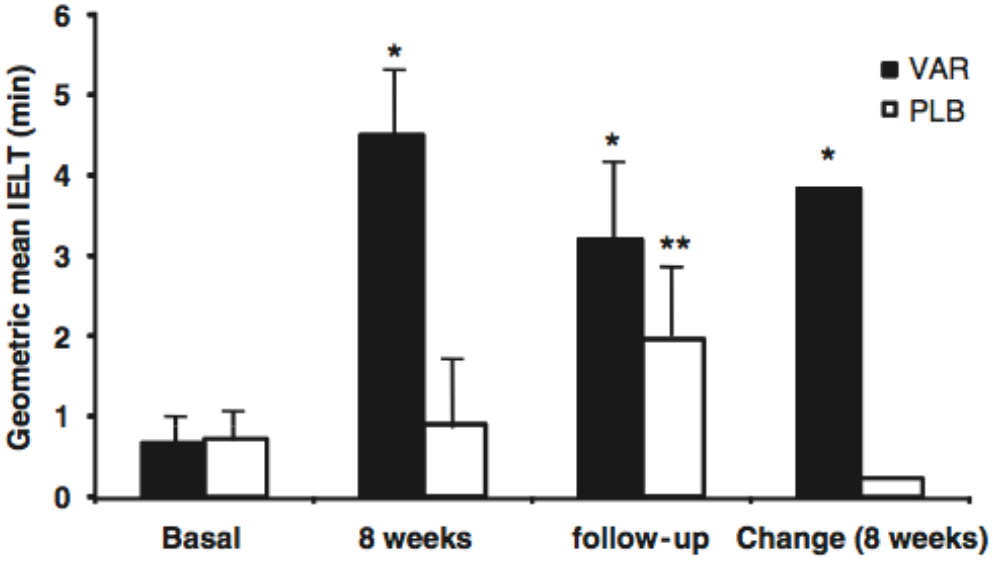
2009

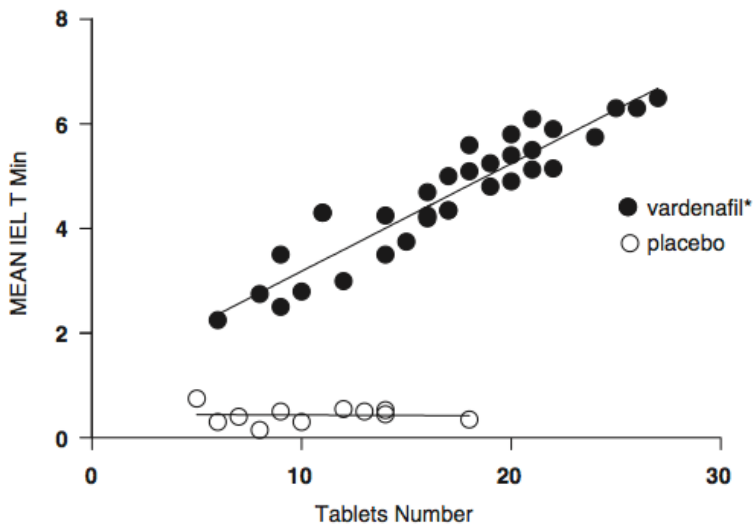
ORIGINAL ARTICLE

Effects of vardenafil administration on intravaginal ejaculatory latency time in men with lifelong premature ejaculation

A Aversa[1], M Pili[1], D Francomano[1], R Bruzziches[1], E Spera[2], G La Pera[3] and G Spera[1]

[1]*Chair of Internal Medicine, DFM, Sapienza University of Rome, Italy;* [2]*Urology Department, Tor Vergata University of Rome, Italy and* [3]*Azienda Ospedaliera San Camillo, Forlanini, Rome, Italy*





A PROSPECTIVE STUDY COMPARING PAROXETINE ALONE VERSUS PAROXETINE PLUS SILDENAFIL IN PATIENTS WITH PREMATURE EJACULATION

ANDREA SALONIA, TOMMASO MAGA, RENZO COLOMBO, VINCENZO SCATTONI, ALBERTO BRIGANTI, ANDREA CESTARI, GIORGIO GUAZZONI, PATRIZIO RIGATTI AND FRANCESCO MONTORSI

From the Department of Urology, University "Vita-Salute" School of Medicine, Scientific Institute H. San Raffaele, Milan, Italy

2002

paroxetine **20 mg** as needed

vs

paroxetine **20 mg** as needed + sildenafil **50 mg** as needed

0,33 min → **3,7 min** p < 0.01 → **4,2 min** p < 0.01

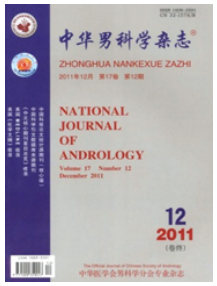
0,35 min → **4,5 min** p < 0.01 → **5,3 min** p < 0.001

△ IELT

3 mesi

6 mesi

Terapia combinata associata a lieve aumento degli effetti collaterali



2005

Comparison between sildenafil plus sertraline and sertraline alone in the treatment of premature ejaculation

Zhang XS, Wang YX, Huang XY, Leng J, Li Z, Han YF

sertraline **50 mg** daily

vs

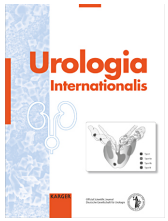
sertraline **50 mg** daily + sildenafil **50 mg** as needed

0,59 min → **3,9 min** p < 0.001

0,56 min → **5,6 min** p < 0.001

△ IELT

Terapia combinata associata a lieve aumento degli effetti collaterali



2008

Tadalafil and fluoxetine in premature ejaculation: prospective, randomized, double-blind, placebo-controlled study

Mattos RM, Marmo Lucon A, Srougi M

fluoxetine + tadalafil	**90 mg** 1/week; **20 mg** as needed	**49 s**	p < 0.001	**336 s**
fluoxetine + placebo	**90 mg** 1/week; as needed	**56 s**	p < 0.001	**233 s**
placebo + tadalafil	1/week; **20 mg** as needed	**49 s**	p = 0.001	**186 s**
placebo + placebo	1/week; as needed	**49 s**	p = 0.042	**46 s**

△ IELT

2014

First International Journal of Andrology
ANDROLOGIA

ORIGINAL ARTICLE

Combination therapy with selective serotonin reuptake inhibitors and phosphodiesterase-5 inhibitors in the treatment of premature ejaculation

E. C. Polat[1], E. Ozbek[2], A. Otunctemur[3], L. Ozcan[4] & A. Simsek[5]

Δ IELT

paroxetine	**20 mg** daily	**60 s**	→	**117 s**	→ **70 s**
tadalafil	**20 mg** as needed	**68 s**	→	**110 s**	→ **79 s**
				$p < 0.01$	
paroxetine + tadalafil	**20 mg** as needed + **20 mg** as needed	**71 s**	→	**175 s**	→ **80 s**

2006

COMPARISON OF EFFICACY OF SILDENAFIL-ONLY, SILDENAFIL PLUS TOPICAL EMLA CREAM, AND TOPICAL EMLA-CREAM-ONLY IN TREATMENT OF PREMATURE EJACULATION

ALI ATAN, M. MURAD BASAR, ALTUG TUNCEL, MEHMET FERHAT, KORAY AGRAS, AND UMIT TEKDOGAN

PATIENT REPORTED SUCCESS RATES

placebo	as needed	**40%**	**8/20 pz**
sildenafil	**50 mg** as needed	**55%**	**11/20 pz**
sildenafil	**50 mg** as needed	**86%**	**19/22 pz**
EMLA	as needed		
EMLA	as needed	**77%**	**17/22 pz**

differenza significativa

differenza non significativa

2012

ORIGINAL RESEARCH—EJACULATORY DISORDERS

Does Current Scientific and Clinical Evidence Support the Use of Phosphodiesterase Type 5 Inhibitors for the Treatment of Premature Ejaculation? A Systematic Review and Meta-analysis

Anastasios D. Asimakopoulos, MD, PhD,* Roberto Miano, MD,† Enrico Finazzi Agrò, MD,† Giuseppe Vespasiani, MD,† and Enrico Spera, MD*

14 studi

- 9 monoterapia con PDE5i
- 4 associazione PDE5i - SSRI
- 1 associazione PDE5i - terapia comportamentale

- 8 sildenafil
- 4 vardenafil
- 2 tadalafil

2012

ORIGINAL RESEARCH—EJACULATORY DISORDERS

Does Current Scientific and Clinical Evidence Support the Use of Phosphodiesterase Type 5 Inhibitors for the Treatment of Premature Ejaculation? A Systematic Review and Meta-analysis

Anastasios D. Asimakopoulos, MD, PhD,* Roberto Miano, MD,† Enrico Finazzi Agrò, MD,† Giuseppe Vespasiani, MD,† and Enrico Spera, MD*

solo EP lifelong

definizioni EP differenti in 11/14

14 studi

1 soddisfa tutti i criteri di studio di livello 1
2 doppio cieco, controllati con placebo, randomizzati
11 varie carenze metodologiche

2012

ORIGINAL RESEARCH—EJACULATORY DISORDERS

Does Current Scientific and Clinical Evidence Support the Use of Phosphodiesterase Type 5 Inhibitors for the Treatment of Premature Ejaculation? A Systematic Review and Meta-analysis

Anastasios D. Asimakopoulos, MD, PhD,* Roberto Miano, MD,† Enrico Finazzi Agrò, MD,† Giuseppe Vespasiani, MD,† and Enrico Spera, MD*

La maggior parte degli studi evidenzia un potenziale effetto dei PDE5i da soli o in associazione con SSRI per il trattamento della EP lifelong

ORIGINAL RESEARCH—EJACULATORY DISORDERS

Does Current Scientific and Clinical Evidence Support the Use of Phosphodiesterase Type 5 Inhibitors for the Treatment of Premature Ejaculation? A Systematic Review and Meta-analysis

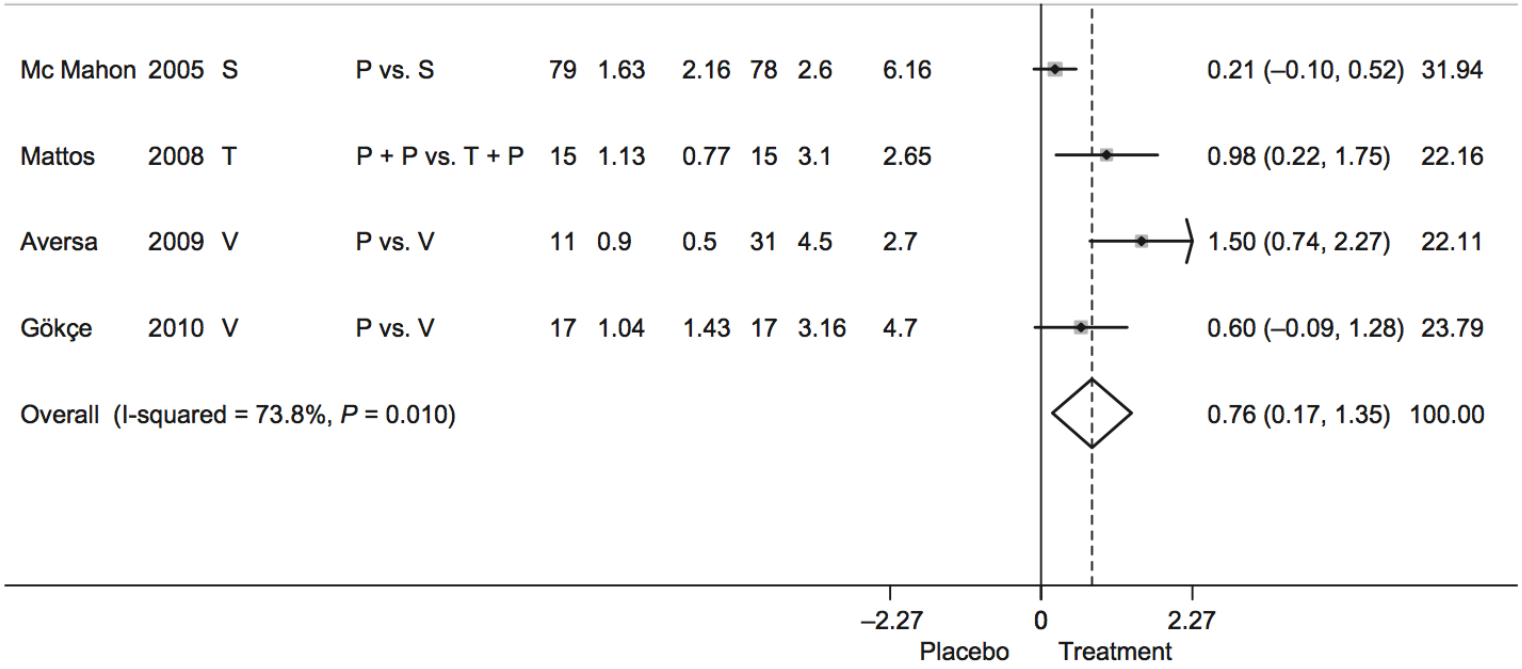
Anastasios D. Asimakopoulos, MD, PhD,* Roberto Miano, MD,† Enrico Finazzi Agrò, MD,† Giuseppe Vespasiani, MD,† and Enrico Spera, MD*

2012

Metanalisi 1

PDE5i **vs** Placebo

Authors	Year	Treatment	Design	Placebo N	Placebo Mean	Placebo SD	Treatment N	Treatment Mean	Treatment SD	SMD (95% CI)	% Weight
Mc Mahon	2005	S	P vs. S	79	1.63	2.16	78	2.6	6.16	0.21 (–0.10, 0.52)	31.94
Mattos	2008	T	P + P vs. T + P	15	1.13	0.77	15	3.1	2.65	0.98 (0.22, 1.75)	22.16
Aversa	2009	V	P vs. V	11	0.9	0.5	31	4.5	2.7	1.50 (0.74, 2.27)	22.11
Gökçe	2010	V	P vs. V	17	1.04	1.43	17	3.16	4.7	0.60 (–0.09, 1.28)	23.79
Overall (I-squared = 73.8%, *P* = 0.010)										0.76 (0.17, 1.35)	100.00

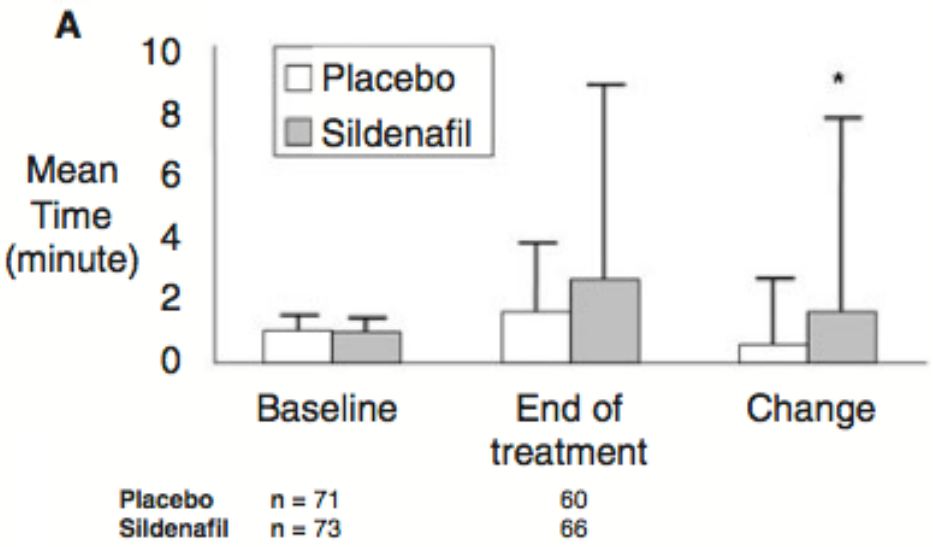


2005

Efficacy of Sildenafil Citrate (Viagra) in Men with Premature Ejaculation

Chris G. McMahon, MB, BS, FACSHP,* Bronwyn G. A. Stuckey, BA, MBBS, FRACP,† Morten Andersen, MD,‡ Kenneth Purvis, MD, PhD,§ Nandan Koppiker, MD, FRCP,¶ Scott Haughie, MSc,¶ and Mitra Boolell, MD¶

*Australian Centre for Sexual Health, Sydney; †Keogh Institute for Medical Research, Sir Charles Gairdner Hospital, Nedlands, Australia; ‡Lillehammer County Hospital, Lillehammer; §Andrologisk Senter, Skoyen Atrium, Oslo, Norway; ¶Pfizer, Sandwich, UK



controllo eiaculatorio

“ejaculatory confidence”

soddisfazione sessuale

periodo refrattario

ORIGINAL RESEARCH—EJACULATORY DISORDERS

Does Current Scientific and Clinical Evidence Support the Use of Phosphodiesterase Type 5 Inhibitors for the Treatment of Premature Ejaculation? A Systematic Review and Meta-analysis

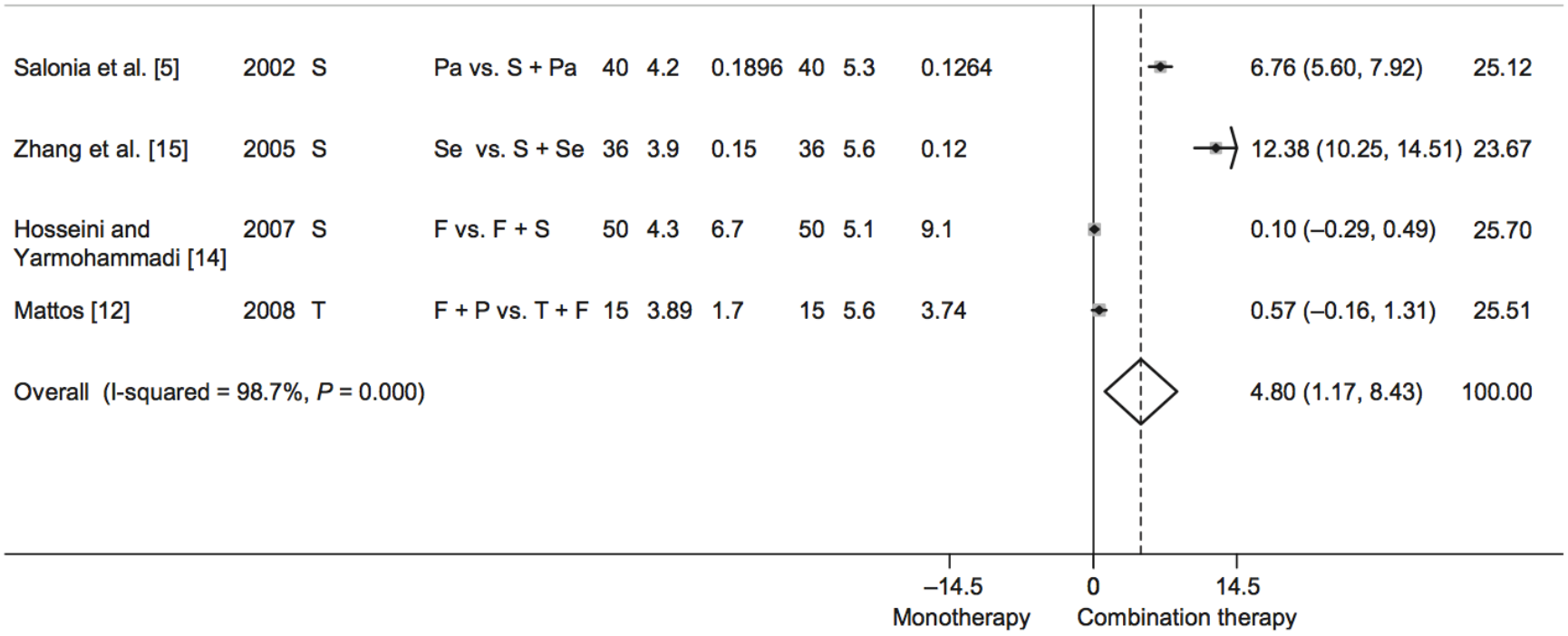
Anastasios D. Asimakopoulos, MD, PhD,* Roberto Miano, MD,† Enrico Finazzi Agrò, MD,† Giuseppe Vespasiani, MD,† and Enrico Spera, MD*

Metanalisi 2

2012

PDE5i **vs** PDE5i + SSRI

Authors	Year	Treatment	Design	Monotherapy N	Monotherapy Mean	Monotherapy SD	Combination therapy N	Combination therapy Mean	Combination therapy SD	SMD (95% CI)	% Weight
Salonia et al. [5]	2002	S	Pa vs. S + Pa	40	4.2	0.1896	40	5.3	0.1264	6.76 (5.60, 7.92)	25.12
Zhang et al. [15]	2005	S	Se vs. S + Se	36	3.9	0.15	36	5.6	0.12	12.38 (10.25, 14.51)	23.67
Hosseini and Yarmohammadi [14]	2007	S	F vs. F + S	50	4.3	6.7	50	5.1	9.1	0.10 (–0.29, 0.49)	25.70
Mattos [12]	2008	T	F + P vs. T + F	15	3.89	1.7	15	5.6	3.74	0.57 (–0.16, 1.31)	25.51
Overall (I-squared = 98.7%, *P* = 0.000)										4.80 (1.17, 8.43)	100.00



2012

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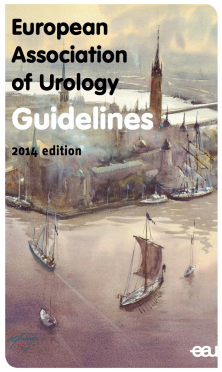
Difetti metodologici nella maggior parte degli studi

Mancanza di una definizione di EP universalmente accettata

Differenti criteri per la valutazione dell'efficacia



2014

Guidelines on Male Sexual Dysfunction:

update 3/2013

Erectile dysfunction and premature ejaculation

K. Hatzimouratidis (chair), I. Eardley, F. Giuliano,
D. Hatzichristou, I. Moncada, A. Salonia, Y. Vardi, E. Wespes

4.8.6.1 Phosphodiesterase type 5 inhibitors

There is only one well-designed, randomized, double-blind, placebo-controlled study comparing sildenafil to placebo (40). Although IELT was not significantly improved, sildenafil increased confidence, the perception of ejaculatory control and overall sexual satisfaction, reduced anxiety and decreased the refractory time to achieve a second erection after ejaculation.

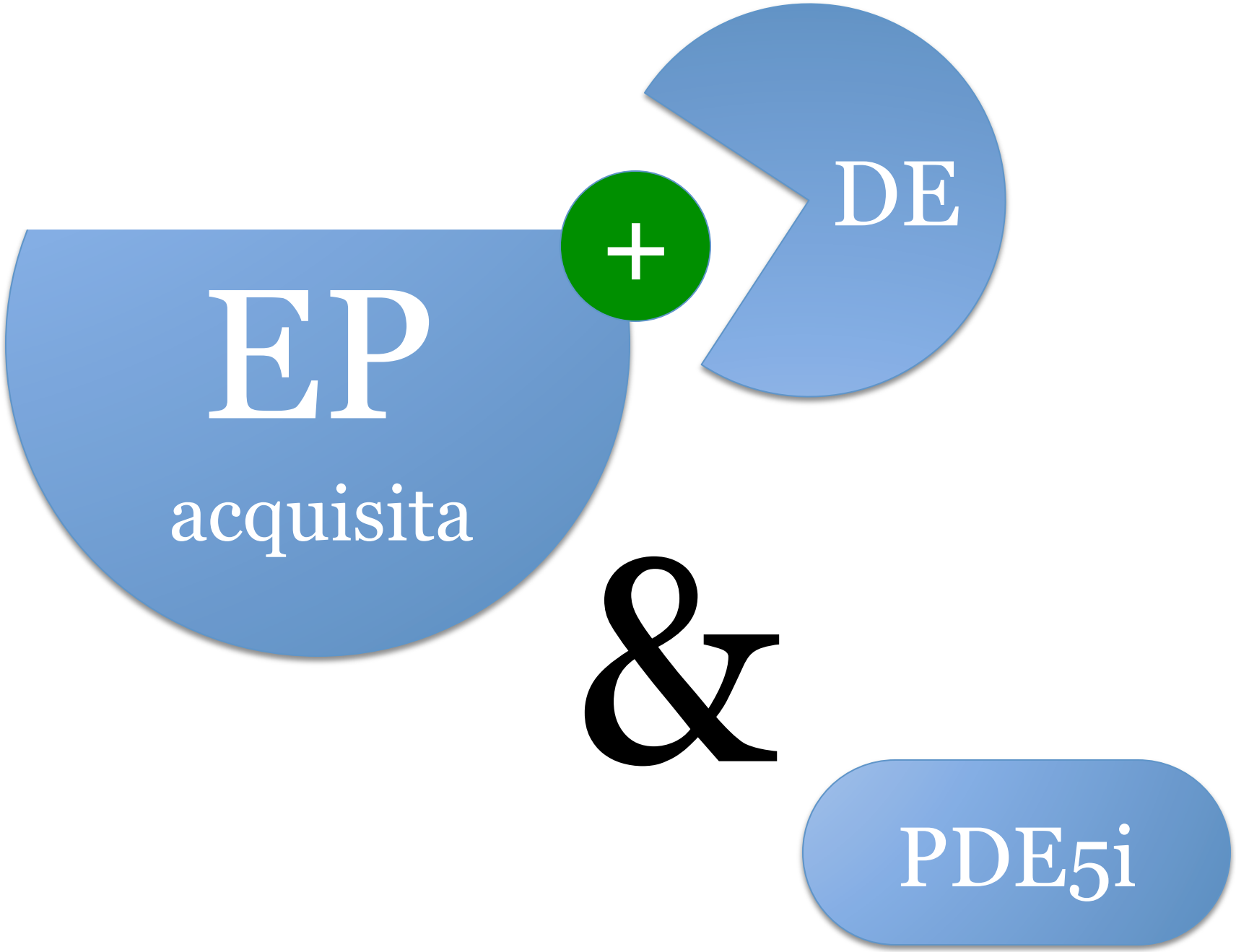
On-demand treatment of PE	**LE**	**GR**
PDE5 inhibitors	3	C

International Society for Sexual Medicine

Summary of recommended pharmacological treatments for premature ejaculation

Drug	Daily dose/ as needed	Dose	IELT fold increase	Side effects	Status	Level of evidence
Oral therapies						
Dapoxetine	As needed	30-60 mg	2.5-3	- Nausea - Diarrhea - Headache - Dizziness	Approved in some countries	1a
Paroxetine	Daily dose	10-40 mg	8	- Fatigue - Yawning - Nausea - Diarrhea - Perspiration - Decreased sexual desire - Erectile dysfunction	Off label	1a
Clomipramine	Daily dose	12.5-50 mg	6		Off label	1a
Sertraline	Daily dose	50-200 mg	5		Off label	1a
Fluoxetine	Daily dose	20-40 mg	5		Off label	1a
Citralopam	Daily dose	20-40 mg	2		Off label	1a
Paroxetine	Daily dose for 30 days and then as needed	10-40 mg	11.6		Off label	1a
Paroxetine	As needed	10-40 mg	1.4		Off label	1a
Clomipramine	As needed	12.5-50 mg	4		Off label	1a
Topical therapy						
Lidocaine/ prilocaine	As needed	25 mg/gm lidocaine 25 mg/gm prilocaine	4-6	- Penile numbness - Partner genital numbness - Skin irritation - Erectile dysfunction	Off label	1b

IELT = Intravaginal Ejaculation Latency Time.


DE
+
EP
acquisita
&
PDE5i

IPOTESI PATOGENETICHE di EP da DE

§ Risposta comportamentale conscia o inconscia alla D.E.

§ Associazione con ansia da prestazione (ipertono adrenergico)

H.S. Kaplan, 1989 – B. Zilbergeld, 1992

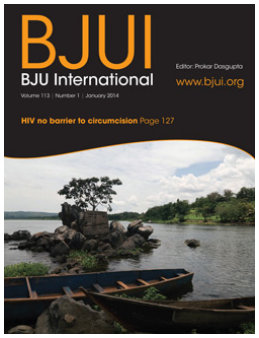
L'ipertono adrenergico attiva l'emissione seminale destabilizzando il controllo del riflesso eiaculatorio

J. Volpe, 1982 – W. Wiliam, 1984

L'ipertono adrenergico riduce la percezione dei segnali prodromici dell'orgasmo

HS. Kaplan, 1989 – B. Zilbergeld, 1992

Può non essere una vera E.P., ma un'eiaculazione da iperstimolazione in caso di reiterati e protratti tentativi di indurre l'erezione



2013

Effects of 12 weeks of tadalafil treatment on ejaculatory and orgasmic dysfunction and sexual satisfaction in patients with mild to severe erectile dysfunction: integrated analysis of 17 placebo-controlled studies[1]

Darius A. Paduch*†, Alexander Bolyakov*†, Paula K. Polzer‡ and Steven D. Watts‡

Department of Urology and Reproductive Medicine, Weill Cornell Medical College, New York, NY, †Consulting Research Services, Inc., Red Bank, NJ, and ‡Lilly Research Laboratories, Eli Lilly, Indianapolis, IN, USA

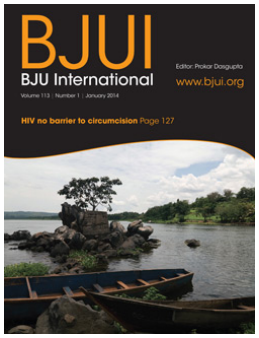
IIEF ejaculation and orgasm domain scores

9. Nelle ultime 4 settimane quando ha avuto una stimolazione sessuale•••• oppure un rapporto sessuale•, quanto spesso ha eiaculato•••?

(0) ❑ non ho avuto alcuna stimolazione sessuale o rapporto sessuale
(5) ❑ quasi sempre o sempre
(4) ❑ la maggior parte delle volte (molto più della metà delle volte)
(3) ❑ qualche volta (circa la metà delle volte)
(2) ❑ poche volte (molto meno della metà delle volte)
(1) ❑ quasi mai o mai

10. Nelle ultime 4 settimane quando ha avuto una stimolazione sessuale•••• oppure un rapporto sessuale•, quanto spesso ha provato la sensazione d'orgasmo con o senza eiaculazione•••?

(0) ❑ non ho avuto alcuna stimolazione sessuale o rapporto sessuale
(5) ❑ quasi sempre o sempre
(4) ❑ la maggior parte delle volte (molto più della metà delle volte)
(3) ❑ qualche volta (circa la metà delle volte)
(2) ❑ poche volte (molto meno della metà delle volte)
(1) ❑ quasi mai o mai



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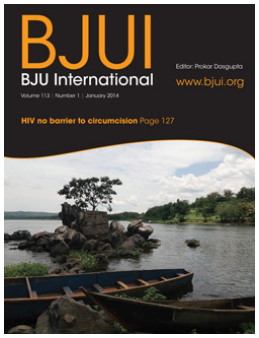
IIEF response	How categorized (severity of EjD or OD)
No intercourse attempts	Not analysed
Never/almost never	Severe
Sometimes/about half the time	Moderate
Always/almost always	Mild/no dysfunction

**IIEF-Q9: 'Over the past 4 weeks, when you had sexual stimulation or intercourse, how often did you ejaculate?' †IIEF-Q10: 'Over the past 4 weeks, when you had sexual stimulation or intercourse, how often did you have the feeling of orgasm with or without ejaculation?'*



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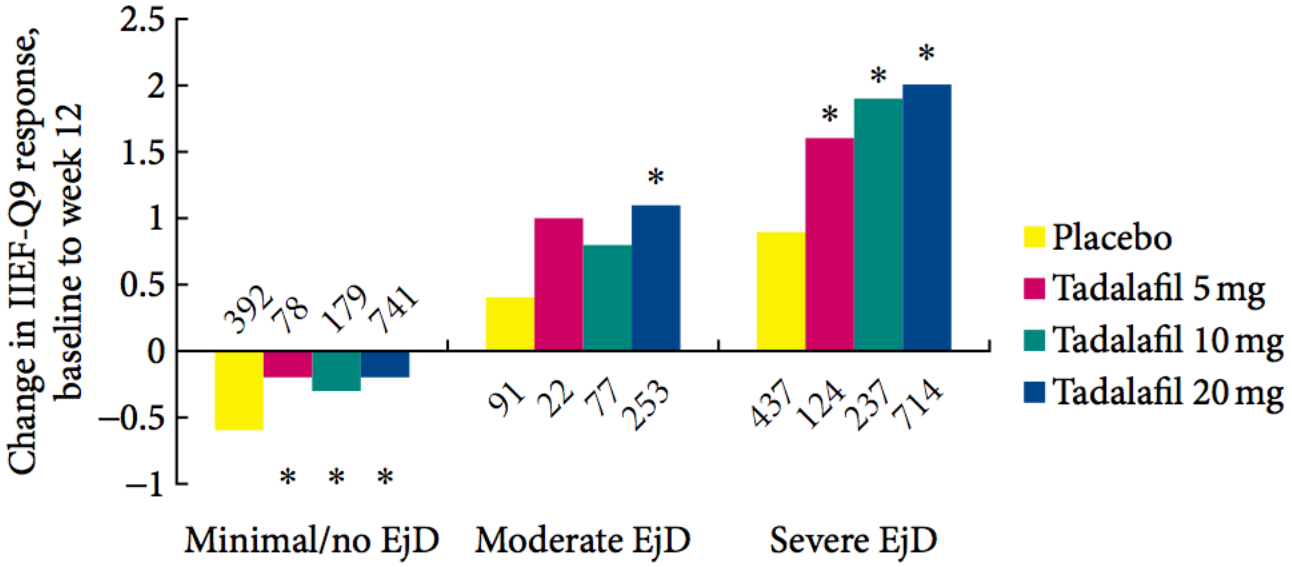

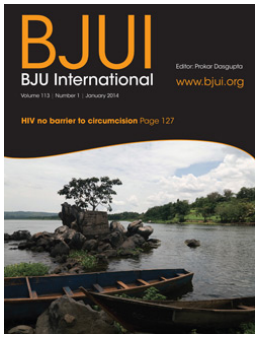

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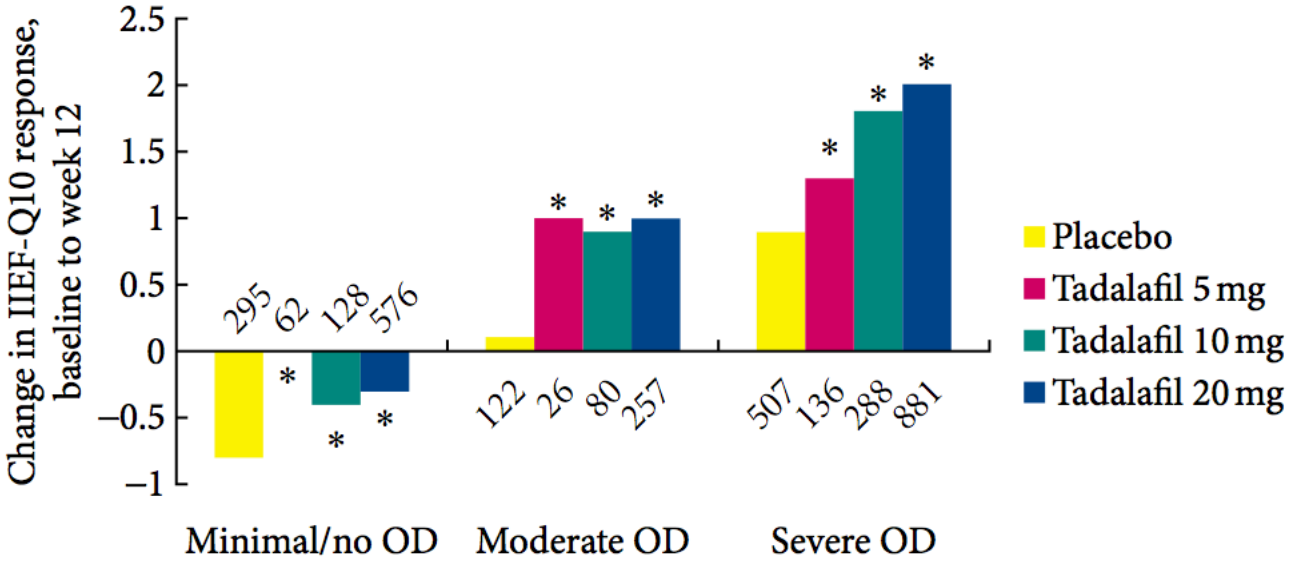

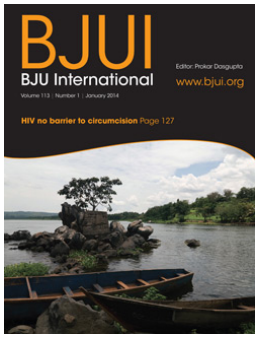

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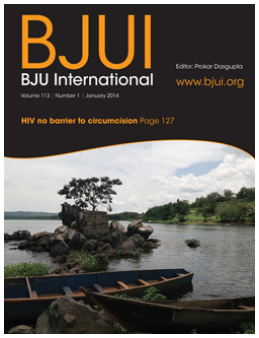
CONCLUSIONI

Il trattamento con tadalafil 10 o 20 mg al bisogno è associato a un significativo miglioramento delle funzioni eiaculatoria e orgasmica (vs placebo) indipendentemente dal grado di DE, disfunzione eiaculatoria o orgasmica.



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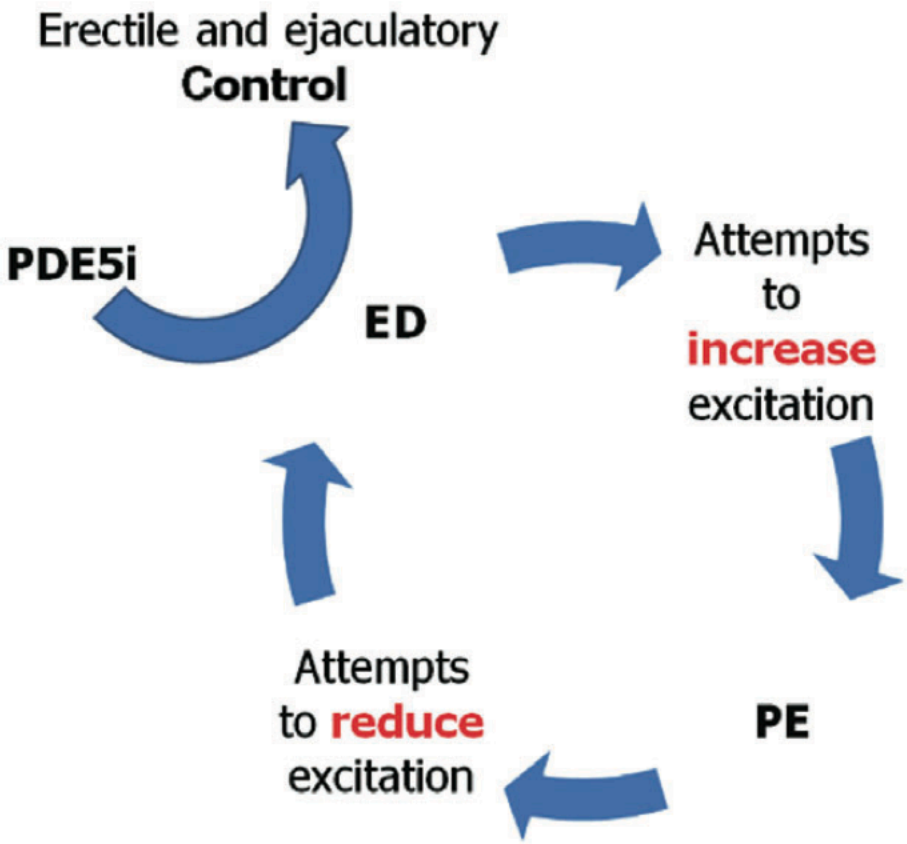
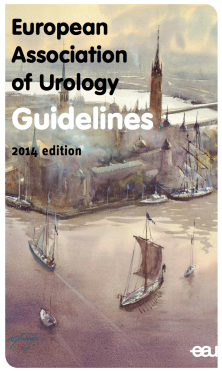
PUNTI DEBOLI

Non ci sono strumenti validati per misurare le diverse dimensioni delle disfunzioni eiaculatorie e dell'orgasmo.

Gli studi presi in considerazione sono stati disegnati per valutare l'efficacia di tadalafil sulla funzione erettile


Erectile and ejaculatory
Control
PDE5i
ED
Attempts
to
increase
excitation
PE
Attempts
to reduce
excitation



2014

Guidelines on Male Sexual Dysfunction:

Erectile dysfunction and premature ejaculation

K. Hatzimouratidis (chair), I. Eardley, F. Giuliano,
D. Hatzichristou, I. Moncada, A. Salonia, Y. Vardi, E. Wespes

update
3/2013

Clinical diagnosis of premature ejaculation based on patient +/- partner history

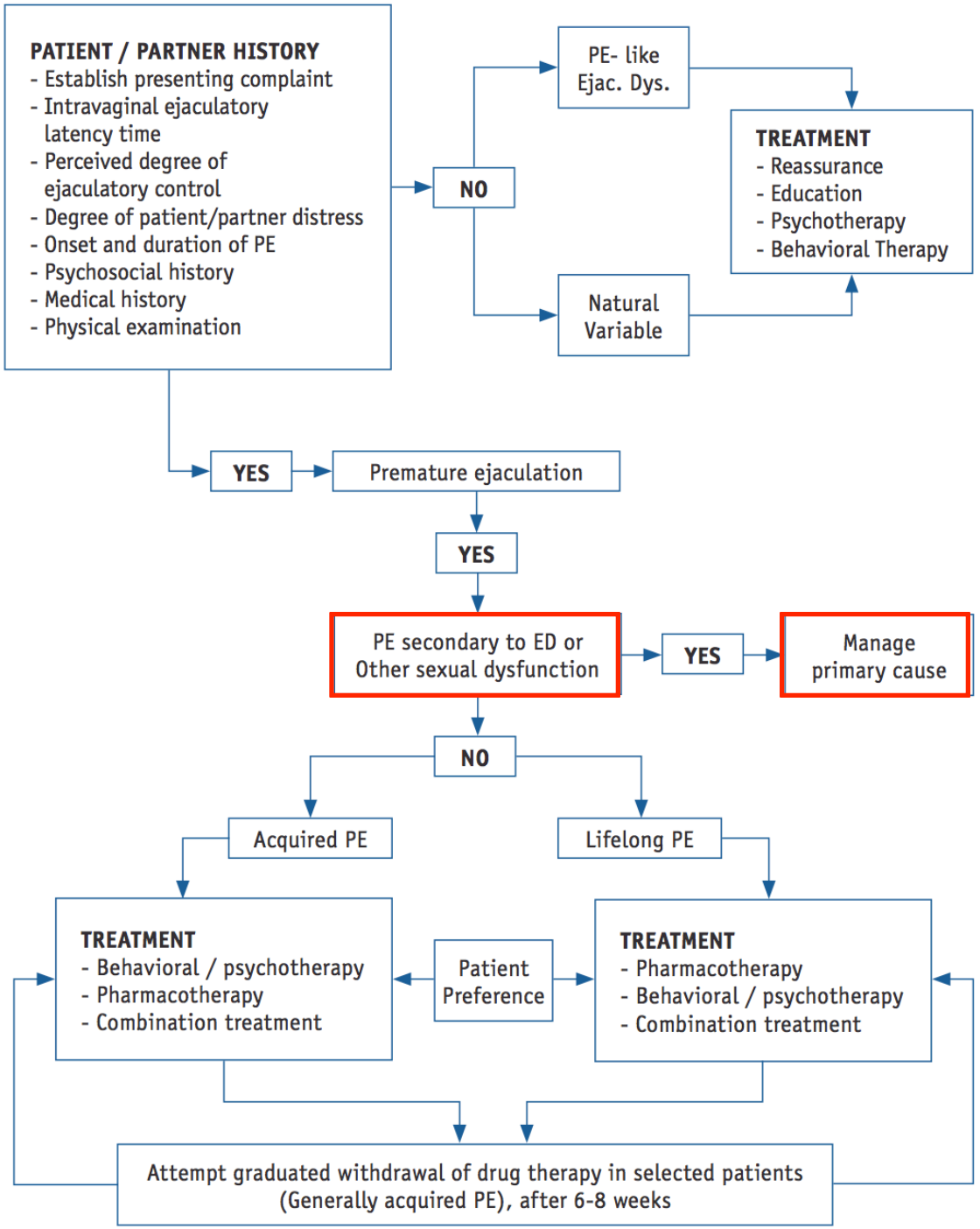
- Time to ejaculation (IELT)
- Perceived degree of ejaculatory control
- Degree of bother/distress
- Onset and duration of PE
- Psychosocial/relationship issues
- Medical history
- Physical examination

Treatment of premature ejaculation

Patient counselling/education
Discussion of treatment options
If PE is secondary to ED, treat ED first or concomitantly

- Pharmacotherapy (recommended as first-line treatment option in lifelong PE)
  - Dapoxetine for on-demand use (the only approved drug for PE)
  - Off-label treatments include chronic daily use of antidepressants (SSRIs or clomipramine) and topical anaesthetics or oral tramadol on demand
- Behavioural therapy, includes stop/start technique, squeeze and sensate focus
- Combination treatment

International Society for Sexual Medicine



2013

Efficacy and Safety of Dapoxetine in Men with Premature Ejaculation and Concomitant Erectile Dysfunction Treated with a Phosphodiesterase Type 5 Inhibitor: Randomized, Placebo-Controlled, Phase III Study

Chris G. McMahon, MBBS, FAChSHM,* Francois Giuliano, MD, PhD,†
John Dean, MBBS, MRCGP, FRCGP,‡ Wayne J.G. Hellstrom, MD, FACS,§ Scott Bull, PharmD,¶
Fisseha Tesfaye, PhD,¶ Om Sharma, PhD,¶ David A. Rivas, MD,¶ and Joseph W. Aquilina, MD¶

TEAE	Placebo (n = 245)	Dapoxetine (n = 250)	*P* value*
Total subjects with TEAE, n (%)	49 (20.0)	74 (29.6)	0.0135
Nausea	3 (1.2)	23 (9.2)	<0.0001
Headache	12 (4.9)	11 (4.4)	0.7924
Diarrhea	2 (0.8)	9 (3.6)	0.0357
Dizziness	2 (0.8)	6 (2.4)	0.1624
Dizziness postural	1 (0.4)	6 (2.4)	0.0606
Upper respiratory tract infection	1 (0.4)	4 (1.6)	0.1849
Vertigo	1 (0.4)	4 (1.6)	0.1849
Dyspepsia	1 (0.4)	3 (1.2)	0.3252
Hyperhidrosis	0	3 (1.2)	0.0855
Insomnia	1 (0.4)	3 (1.2)	0.3252
Nasopharyngitis	4 (1.6)	3 (1.2)	0.6836
Flushing	3 (1.2)	0	0.0793
Nasal congestion	3 (1.2)	0	0.0793

Sincope: 2 casi (0,8%) nel gruppo dapoxetina

- ritardata
- inibita
- impotentia eiaculationis
- aneiaculazione
- anorgasmia

EIACULAZIONE RITARDATA/ANEIACULAZIONE

DSM-IV-TR
Persistente o ricorrente ritardo, o assenza, dell'orgasmo in seguito a una normale fase di eccitazione durante l'attività sessuale che il clinico, considerando l'età del soggetto, giudica adeguata in termini di qualità, intensità e durata. Il disturbo causa considerevole distress o difficoltà interpersonali.

WHO 2nd Consultation on Sexual Dysfunction
Persistente o ricorrente difficoltà, ritardo o impossibilità di raggiungere l'orgasmo in seguito a sufficiente stimolazione sessuale, che causa un personale distress

EIACULAZIONE RITARDATA/ANEIACULAZIONE

Non esistono criteri precisi per stabilire quando un paziente è affetto da eiaculazione ritardata

Considerato che la maggior parte degli uomini sessualmente attivi eiacula in un intervallo compreso tra 4 e 10 minuti, il clinico può assumere che gli uomini che presentano latenze di oltre 25 minuti e che riferiscono distress, oppure gli uomini che cessano l'attività sessuale per esaurimento o irritazione, presentino una eiaculazione ritardata.

EIACULAZIONE RITARDATA/ANEIACULAZIONE

Prevalenza 1.5/1000
Non superiore al 3%

25% lifelong
75% acquisita

Nella maggior parte dei casi: nessuna evidenza di chiara eziologia somatica

CAUSE	
Psychogenic	Inhibited ejaculation
Congenital	Mullerian duct cyst Wolfian duct abnormality Prune belly syndrome
Anatomic Causes	Transurethral resection of prostate Bladder neck incision
Neurogenic Causes	Diabetic autonomic neuropathy Spinal cord injury Radical cystectomy or prostatectomy Proctocolectomy Bilateral sympathectomy Abdominal aortic aneurysmectomy Para-aortic lympthadenectomy
Infective	Urethritis Genito–urinary tuberculosis Schistosomiasis
Endocrine	Hypogonadism Hypothyroidism
Medication	Alpha-methyl dopa Thiazide diuretics Tricyclic and SSRI antidepressants Phenothiazine Alcohol abuse

EIACULAZIONE RITARDATA/ANEIACULAZIONE

OFF-LABEL

Alfa-1 agonisti
Ciproeptadina
Amantadina
Buspirone
Bupropione
Yohimbina
Apomorfina
Quinerolane
Ossitocina

EIACULAZIONE RITARDATA/ANEIACULAZIONE

Alti livelli di:
- distress personale e relazionale
- insoddisfazione sessuale
- ansia da prestazione sessuale
- problemi di salute generale

Caratteristica comune: nessuna difficoltà nell'erezione

In alcuni casi però… il timore di non riuscire ad eiaculare e la conseguente ansia possono distrarre l'attenzione dagli spunti erotici che servono ad alimentare l'eccitazione

PDE5i


retrograda

EIACULAZIONE RETROGRADA

CAUSE
- anatomiche
- neurologiche
- farmacologiche
- idiopatiche

TERAPIA FARMACOLOGICA
- per cause ad eziologia neurologica
- alfa agonisti
- antidepressivi triciclici con attività anticolinergica

dolorosa

EIACULAZIONE DOLOROSA

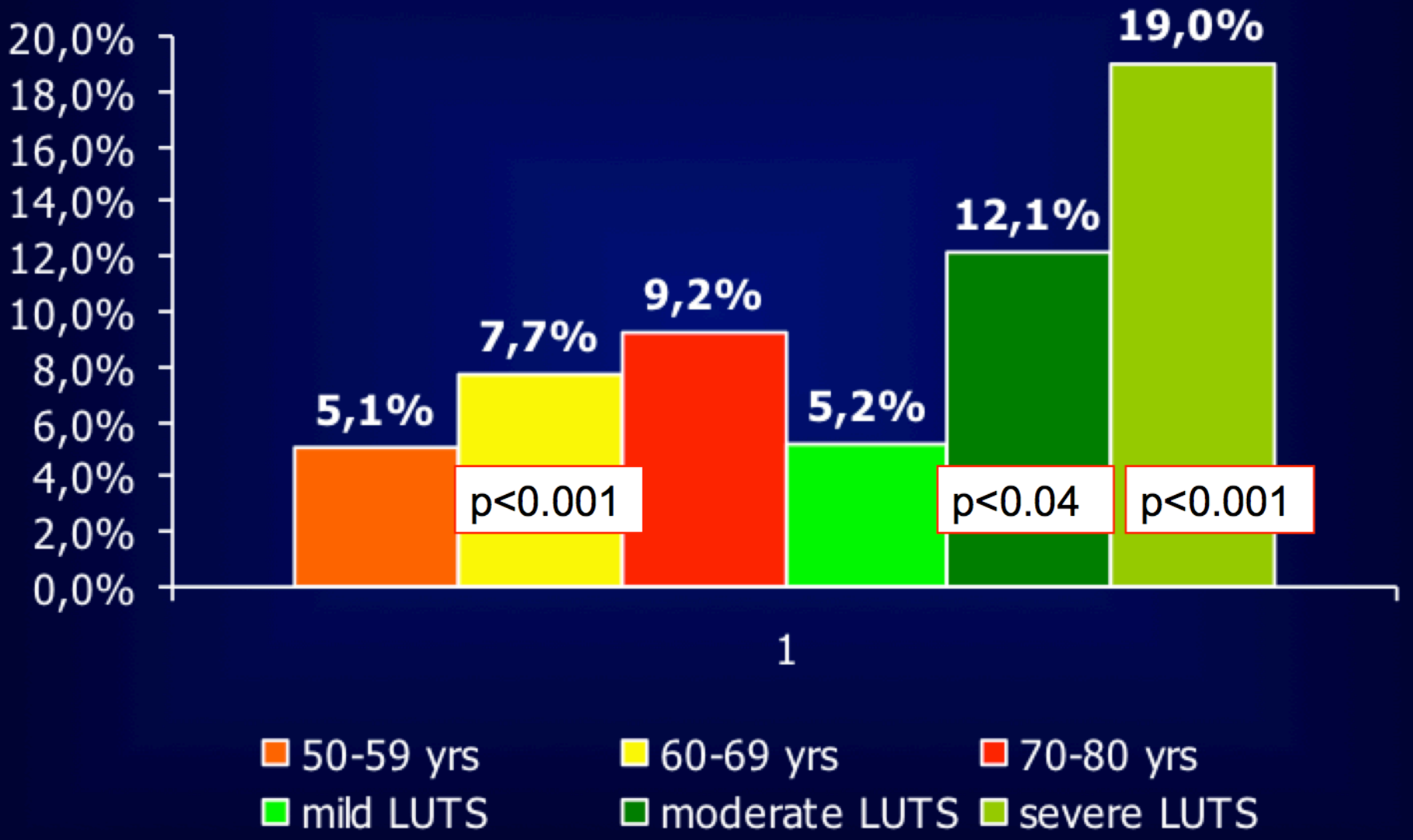
Prevalenza 6,7%

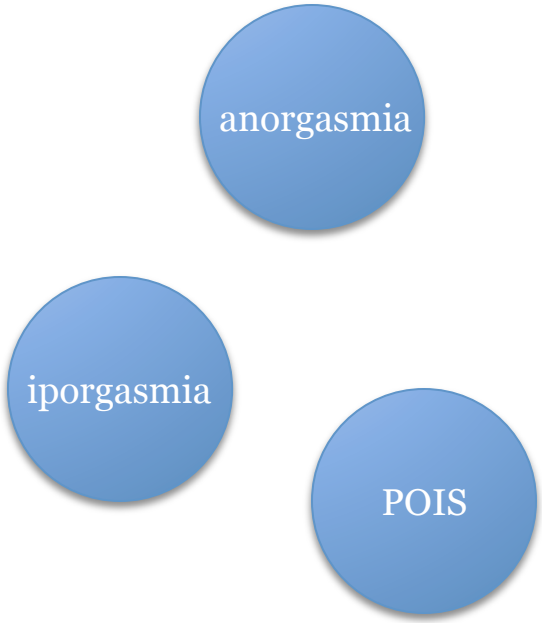
CAUSE
- IPB
- alfa-litici
- prostatite/vescicolite
- dolore pelvico cronico
- litiasi delle vescicole seminali
- ostruzione dei dotti eiaculatori
- antidepressivi triciclici e SSRI

Painful Ejaculation: 6.7%

Rosen RC, et al. Eur Urol, 44:637-649, 2003

Prevalence of painful Ej




anorgasmia
iporgasmia
POIS

ORGASMO

La percezione delle contrazioni della muscolatura striata e dell'espulsione del liquido seminale durante l'eiaculazione, mediata attraverso i neuroni sensitivi della regione pelvica

Distinto evento corticale, che origina un'esperienza cognitiva e emozionale

Il risultato della processazione cerebrale di stimoli sensoriali mediati dal nervo pudendo, risultanti dall'aumento della pressione nell'uretra posteriore, dalle contrazioni del bulbo uretrale e delle ghiandole genitali accessorie

2005

0022-5347/05/1736-2067/0
THE JOURNAL OF UROLOGY®

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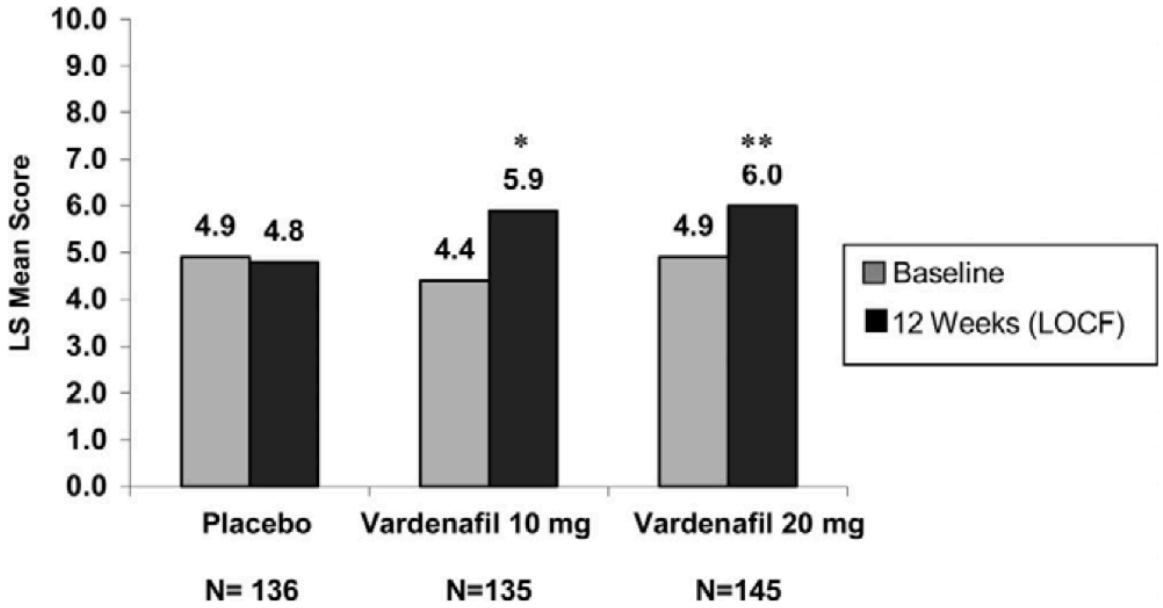
Printed in U.S.A.
DOI: 10.1097/01.ju.0000158456.41788.93

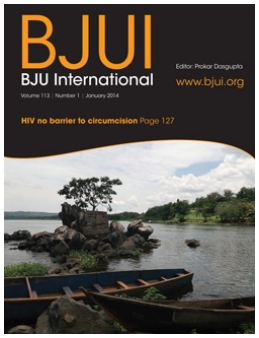
VARDENAFIL IMPROVED PATIENT SATISFACTION WITH ERECTILE HARDNESS, ORGASMIC FUNCTION AND SEXUAL EXPERIENCE IN MEN WITH ERECTILE DYSFUNCTION FOLLOWING NERVE SPARING RADICAL PROSTATECTOMY

AJAY NEHRA,* JOHN GRANTMYRE,† ANDREA NADEL,† MARC THIBONNIER† AND GERALD BROCK‡

From the Department of Urology, Mayo Clinic (AN), Rochester, Minnesota, Dalhousie University (JG), Halifax, Nova Scotia, and Lawson Research Institute, St. Joseph's Health Centre, University of Western Ontario (GB), London, Ontario, Canada, and Bayer Pharmaceuticals Corp. (AN, MT), West Haven, Connecticut

IIEF orgasmic function domain scores





2007

The utility of sildenafil citrate for infertile men with sexual dysfunction: a pilot study

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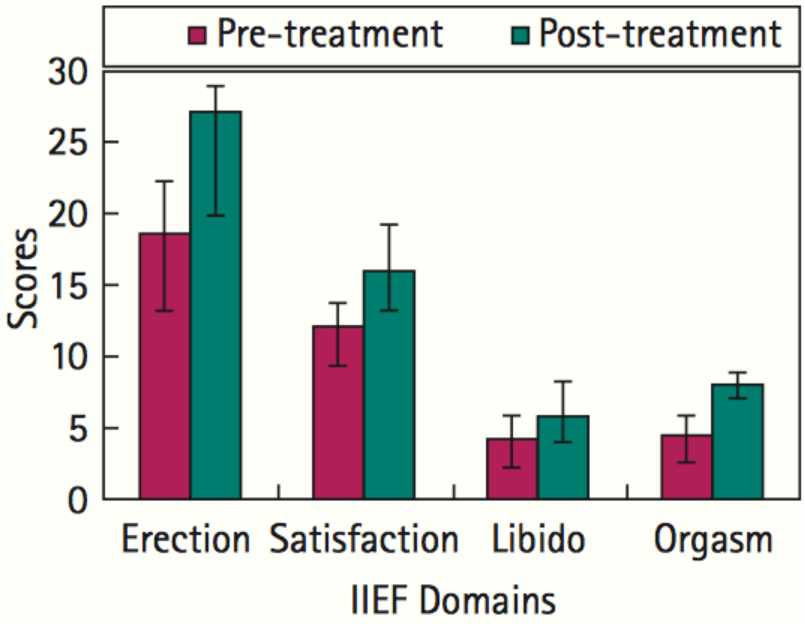

IIEF orgasm domain scores

10. Nelle ultime 4 settimane quando ha avuto una stimolazione sessuale•••• **oppure** un rapporto sessuale•, quanto spesso ha provato la sensazione d'orgasmo con o senza eiaculazione•••?

(0) ❑ non ho avuto alcuna stimolazione sessuale o rapporto sessuale
(5) ❑ quasi sempre o sempre
(4) ❑ la maggior parte delle volte (molto più della metà delle volte)
(3) ❑ qualche volta (circa la metà delle volte)
(2) ❑ poche volte (molto meno della metà delle volte)
(1) ❑ quasi mai o mai

8. Nelle ultime 4 settimane quanto piacevoli sono stati per lei i suoi rapporti sessuali•?

(0) ❑ non ho avuto alcun rapporto sessuale
(5) ❑ estremamente piacevoli
(4) ❑ molto piacevoli
(3) ❑ abbastanza piacevoli
(2) ❑ non molto piacevoli
(1) ❑ per niente piacevoli

PDE5i & EP

NO nell'SNC e SNP agisce aumentando la latenza eiaculatoria

PDE5i sono stati valutati per un potenziale trattamento dei disturbi eiaculatori, soprattutto l'EP

Sildenafil è il PDE5i più studiato per la terapia dell'EP

Efficacia PDE5i da soli o associati a SSRI per EP lifelong: bassi livelli di evidenza

PDE5i sembrano potenziare effetto degli SSRI

PDE5i + dapoxetina: associazione sicura

LG:	EP lifelong	basso grado di raccomandazione
	EP +DE	PDE5i prima scelta

Per ora scarse informazioni